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(54) Title: 2,3-SUBSTITUTED INDOLE COMPOUNDS AS COX-2 INHIBITORS			
<p style="text-align: center;">(I)</p>			
(57) Abstract			
<p>This invention provides a compound of formula (I) or the pharmaceutically acceptable salts thereof wherein Z is OH, C<sub>1-6</sub> alkoxy, -NR<sup>2</sup>R<sup>3</sup> or heterocycle; Q is selected from the following: (a) an optionally substituted phenyl, (b) an optionally substituted 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), (c) an optionally substituted 5-membered aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, (d) an optionally substituted C<sub>3-7</sub> cycloalkyl and (e) an optionally substituted benzofused heterocycle; R<sup>1</sup> is hydrogen, C<sub>1-4</sub> alkyl or halo; R<sup>2</sup> and R<sup>3</sup> are independently hydrogen, OH, C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkyl substituted with halo, OH, C<sub>1-4</sub> alkoxy or CN; X is independently selected from H, halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino and CN; and n is 0, 1, 2, 3 and 4. This invention also provides a pharmaceutical composition useful for the treatment of a medical condition in which prostaglandins are implicated as pathogens.</p>			

## 2,3-SUBSTITUTED INDOLE COMPOUNDS AS COX-2 INHIBITORS

Technical Field

- This invention relates to novel 2,3-substituted indoles as pharmaceutical agents.
- 5 This invention specifically relates to compounds, compositions and methods for the treatment or alleviation of pain and inflammation and other inflammation-associated disorders, such as arthritis.

Background Art

Nonsteroidal antiinflammatory drugs (NSAIDs) are widely used in treating pain and the signs and symptoms of arthritis because of their analgesic and anti-inflammatory activity. It is accepted that common NSAIDs work by blocking the activity of cyclooxygenase (COX), also known as prostaglandin G/H synthase (PGHS), the enzyme that converts arachidonic acid into prostanoids. Prostaglandins, especially prostaglandin E<sub>2</sub> (PGE<sub>2</sub>), which is the predominant eicosanoid detected in inflammation conditions, are mediators of pain, fever and other symptoms associated with inflammation. Inhibition of the biosynthesis of prostaglandins has been a therapeutic target of anti-inflammatory drug discovery. The therapeutic use of conventional NSAIDs is, however, limited due to drug associated side effects, including life threatening ulceration and renal toxicity. An alternative to NSAIDs is the use of corticosteroids, however, long term therapy can also result in severe side effects.

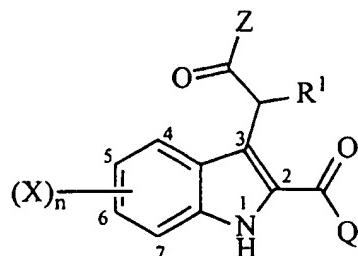
Recently, two forms of COX were identified, a constitutive isoform (COX-1) and an inducible isoform (COX-2) of which expression is upregulated at sites of inflammation (Vane, J. R.; Mitchell, J. A.; Appleton, I.; Tomlinson, A.; Bishop-Bailey, D.; Croxtoll, J.; Willoughby, D. A. *Proc. Natl. Acad. Sci. USA*, 1994, 91, 2046). COX-1 is thought to play a physiological role and to be responsible for gastrointestinal and renal protection. On the other hand, COX-2 appears to play a pathological role and to be the predominant isoform present in inflammation conditions. A pathological role for prostaglandins has been implicated in a number of human disease states including rheumatoid and osteoarthritis, pyrexia, asthma, bone resorption, cardiovascular diseases, nephrotoxicity, atherosclerosis, hypotension, shock, pain,

cancer, and Alzheimer disease. The NSAIDs currently on market inhibit both isoforms of COX with little variation for selectivity, explaining their beneficial (inhibition of COX-2) and deleterious effects (inhibition of COX-1). It is believed that compounds that would selectively inhibit the biosynthesis of prostaglandins by intervention of the induction phase of the inducible enzyme cyclooxygenase-2 and/or by intervention of the activity of the enzyme cyclooxygenase-2 on arachidonic acid would provide alternate therapy to the use of NSAIDs or corticosteroids in that such compounds would exert anti-inflammatory effects without the adverse side effects associated with COX-1 inhibition.

A variety of indole compounds are known and are disclosed in several patent applications. The International Publication Numbers WO 96/32379 discloses N-substituted indole compounds as cGMP-PDE Inhibitors. The International Publication Numbers WO 96/37467, WO 96/37469, UK Patent Publication GB 2283745 A and US Publication Number 5510368 disclose 2-methyl-N-substituted indole compounds as cyclooxygenase-2 Inhibitors. Also, a variety of indole compounds are disclosed as agents for controlling underwater fouling organisms in European Patent Publication Number 0 556 949 A2 by Konya, Kazumi et al. Specifically, the International Publication Numbers WO 97/09308 discloses indole compounds as neuropeptide receptor antagonists. Besides, in Sci. Pharm. 64, 577 (1996), a process for preparing a 2-ester-substituted indoline is disclosed.

#### Brief Disclosure of the Invention

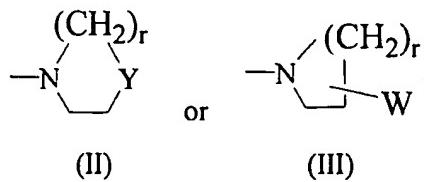
The present invention provides a compound of the following formula:



(I)

or the pharmaceutically acceptable salts thereof wherein

Z is OH, C<sub>1-6</sub> alkoxy, -NR<sup>2</sup>R<sup>3</sup> or a group of the formula (II) or (III):



wherein r is 1, 2, 3 or 4, Y is a direct bond, O, S or NR<sup>4</sup>, and W is OH or -NR<sup>2</sup>R<sup>3</sup>;

**Q** is selected from the following:

- 5           (a) phenyl optionally substituted with one; two or three substituents independently selected from

10          (a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>R<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl,

15          (a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

20          (a-3) 5-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

25          (a-4) 6-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

30          (b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently

selected from the above group (a-1), (a-2), (a-3) and (a-4);

- (c) a 5-membered monocyclic aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);
- (d) C<sub>3-7</sub> cycloalkyl optionally substituted with one or two substituents independently selected from OH, C<sub>1-4</sub> alkyl, halo and halo-substituted C<sub>1-4</sub> alkyl; and
- (e) a benzo-fuzed heterocycle optionally substituted with one, two or three substituents independently selected from the group (a-1);

R<sup>1</sup> is hydrogen, C<sub>1-4</sub> alkyl or halo;

R<sup>2</sup> and R<sup>3</sup> are independently H, OH, C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkyl substituted with halo, OH, C<sub>1-4</sub> alkoxy, NH<sub>2</sub> or CN;

R<sup>4</sup> is hydrogen or C<sub>1-4</sub> alkyl;

X is independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>NR<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl; and

n is 0, 1, 2, 3 or 4.

The indole compounds of the present invention exhibit inhibition of COX activity. Preferably compounds of this invention exhibit inhibitory activity against COX-2, with more preferable compounds having COX-2 selectivity.

Accordingly, the present invention also provides a pharmaceutical composition, useful for the treatment of a medical condition in which prostaglandins are implicated as pathogens, which comprises a compound of the formula (I) and the pharmaceutically acceptable salts thereof.

Further, the present invention provides a method for the treatment of a medical condition in which prostaglandins are implicated as pathogens, in a mammalian subject.

which comprises administering to said subject a therapeutically effective amount of said pharmaceutical composition.

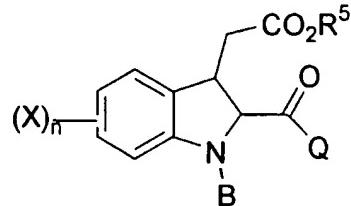
The medical conditions in which prostaglandins are implicated as pathogens, include the relief of pain, fever and inflammation of a variety of conditions including 5 rheumatic fever, symptoms associated with influenza or other viral infections, common cold, low back and neck pain, dysmenorrhea, headache, toothache, sprains and strains, myositis, neuralgia, synovitis, arthritis including rheumatoid arthritis, degenerative joint disease (osteoarthritis), gout, ankylosing spondylitis, systemic lupus erythematosus and juvenile arthritis, bursitis, burns, injuries following surgical and 10 dental procedures.

The compounds and pharmaceutical composition of this invention may inhibit cellular neoplastic transformations and metastatic tumor growth and thus may be used in the treatment and/or prevention of cancers in the colon, breast, skin, esophagus, stomach, urinary bladder, lung and liver. The compounds and pharmaceutical 15 composition of this invention were used in the treatment and/or prevention of cyclooxygenase-mediated proliferation disorders such as which occur in diabetic retinopathy and tumor angiogenesis.

The compounds and pharmaceutical composition of this invention may inhibit prostaniod-induced smooth muscle contraction by preventing the synthesis of 20 contractile prostanoids, and thus may be of use in the treatment of dysmenorrhea, premature labor, asthma and eosinophil related disorders and in the treatment of neurodegenerative diseases such as Alzheimer's and Parkinson's disease, and for the treatment of bone loss (treatment of osteoarthritis), stroke, seizures, migraine, multiple sclerosis, AIDS and encephalopathy.

25 By virtue of the COX-2 activity and/or specificity for COX-2 over COX-1, such compounds will prove useful as an alternative to conventional NSAIDs particularly where such NSAIDs may be contra-indicated such as in patients with ulcers (such as peptic ulcers and gastric ulcers), gastritis, regional enteritis, ulcerative colitis, diverticulitis or with a recurrent history of GI lesions, GI bleeding, coagulation 30 disorders including anemia such as hypoprothrombinemia, haemophilia and other bleeding problems; kidney disease; prior to surgery of taking of anticoagulants.

Also, the present invention provides a compound of formula 7-VI:



7-VI

wherein **B** is a suitable protecting group;

5   **Q** is selected from the following:

- (a) phenyl optionally substituted with one, two or three substituents independently selected from
  - (a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>1-4</sub> cycloalkyl,
  - (a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
  - (a-3) 5-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
  - (a-4) 6-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub>

alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

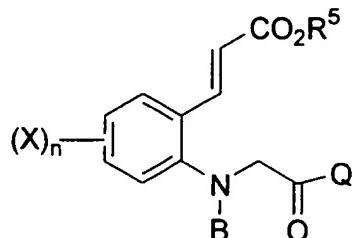
- (b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),
- 5 (c) a 5-membered monocyclic aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);
- 10 (d) C<sub>3-7</sub> cycloalkyl optionally substituted with one or two substituents independently selected from OH, C<sub>1-4</sub> alkyl, halo and halo-substituted C<sub>1-4</sub> alkyl; and
- 15 (e) a benzo-fused heterocycle optionally substituted with one, two or three substituents independently selected from the group (a-1);

**R<sup>2</sup>** and **R<sup>3</sup>** are independently H, OH, C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkyl substituted with halo, OH, C<sub>1-4</sub> alkoxy, NH<sub>2</sub> or CN;

**X** is independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>NR<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl; **R<sup>5</sup>** is C<sub>1-6</sub> alkyl; and

**n** is 0, 1, 2, 3 or 4.

25 Also, the present invention provides a compound of formula 7-V:



7-V

wherein B is a suitable protecting group;

**Q** is selected from the following:

- 5 (a) phenyl optionally substituted with one, two or three substituents independently selected from

10 (a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl,

15 (a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

20 (a-3) 5-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

25 (a-4) 6-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

30 (b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),

(c) a 5-membered monocyclic aromatic group containing one heteroatom

selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);

- (d)  $C_{3-7}$  cycloalkyl optionally substituted with one or two substituents independently selected from OH,  $C_{1-4}$  alkyl, halo and halo-substituted  $C_{1-4}$  alkyl; and
- (e) a benzo-fuzed heterocycle optionally substituted with one, two or three substituents independently selected from the group (a-1);

10  $R^2$  and  $R^3$  are independently H, OH,  $C_{1-4}$  alkoxy,  $C_{1-4}$  alkyl or  $C_{1-4}$  alkyl substituted with halo, OH,  $C_{1-4}$  alkoxy,  $NH_2$  or CN;

X is independently selected from halo,  $C_{1-4}$  alkyl, halo-substituted  $C_{1-4}$  alkyl, OH,  $C_{1-4}$  alkoxy, halo-substituted  $C_{1-4}$  alkoxy,  $C_{1-4}$  alkylthio,  $NO_2$ ,  $NH_2$ , di-( $C_{1-4}$  alkyl)amino, 15  $C_{1-4}$  alkylamino, CN, HO-( $C_{1-4}$ ) alkyl,  $C_{1-4}$  alkoxy- $C_{1-4}$  alkyl,  $C_{1-4}$  alkylsulfonyl, aminosulfonyl, - $NH_2S(O)_2NR^2NR^3$ , acetyl, -COOH, -C(O)O- $C_{1-4}$  alkyl,  $C_{1-4}$  alkylsulfonylamino and  $C_{3-7}$  cycloalkyl;  $R^5$  is  $C_{1-6}$  alkyl; and

n is 0, 1, 2, 3 or 4.

#### Detailed Disclosure of the Invention

20 As used herein, "halo" is fluoro, chloro, bromo or iodo.

As used herein, the term " $C_{1-4}$  alkyl" means straight or branched chain saturated radicals of 1 to 4 carbon atoms, including, but not limited to methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, and the like.

As used herein, an example of "propyl" is n-propyl and isopropyl.

25 As used herein, an example of "butyl" is n-butyl, isobutyl, sec-butyl and tert-butyl.

As used herein, an example of "alkoxy" is methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy, sec-butoxy, tert-butoxy, and the like.

30 As used herein, an example of "alkylthio" is methylthio, ethylthio, n-propylthio, isopropylthio, n-butylthio, isobutylthio, sec-butylthio, tert-butylthio, and the like.

As used herein, an example of "di-( $C_{1-4}$  alkyl)amino" is dimethylamino,

diethylamino, dipropylamino, N-methyl-N-ethylamino, N-methyl-N-propylamino, N-methyl-N-butylamino, N-ethyl-N-propylamino, and the like.

As used herein, an example of "C<sub>1-4</sub> alkylamino" is methylamino, ethylamino, n-propylamino, isopropylamino, n-butylamino, isobutylamino, *sec*-butylamino, *tert*-butylamino, and the like.

As used herein, an example of "HO-(C<sub>1-4</sub>)alkyl" is hydroxymethyl, hydroxyethyl (e.g., 1-hydroxyethyl and 2-hydroxyethyl), hydroxypropyl (e.g., 1-hydroxypropyl, 2-hydroxypropyl and 3-hydroxypropyl)

As used herein, an example of "C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl" is methoxymethyl, 10 methoxyethyl, methoxypropyl, methoxybutyl, ethoxymethyl, ethoxyethyl, ethoxypropyl, and the like.

As used herein, the term "halo-substituted alkyl" refers to an alkyl radical as described above substituted with one or more halogens included, but not limited to, chloromethyl, dichloromethyl, fluoromethyl, difluoromethyl, trifluoromethyl, 2,2,2-trichloroethyl, and the like.

As used herein, an example of "halo-substituted alkoxy" is chloromethoxy, dichloromethoxy, fluoromethoxy, difluoromethoxy, trifluoromethoxy, 2,2,2-trichloroethoxy, and the like.

As used herein, the term "C<sub>3-7</sub> cycloalkyl" means carbocyclic radicals, of 3 to 20 carbon atoms, including, but not limited to cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and the like.

As used herein, an example of "aryl" is phenyl and naphthyl.

As used herein, a 5-membered monocyclic aromatic group usually has one heteroatom selected from O, S and N in the ring. In addition to said heteroatom, the 25 monocyclic aromatic group may optionally have up to three N atoms in the ring. For example, the 5-membered monocyclic aromatic group includes thieryl, furyl, thiazolyl (e.g., 1,3-thiazolyl, 1,2-thiazolyl), imidazolyl, pyrrolyl, oxazolyl (e.g., 1,3-oxazolyl, 1,2-oxazolyl, isoxazolyl), pyrazolyl, tetrazolyl, triazolyl (e.g., 1,2,3-triazolyl, 1,2,4-triazolyl), oxadiazolyl (e.g., 1,2,3-oxadiazolyl), thiadiazolyl (e.g., 1,3,4-thiadiazolyl, 30 1,2,3-thiadiazolyl) and the like.

As used herein, an example of a 6-membered monocyclic aromatic group

includes pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazinyl (e.g., 1,3,5-triazinyl), tetrazinyl and the like.

- As used herein, an example of a benzo-fuzed heterocycle includes quinolyl, isoquinolyl, cinnolinyl, quinoxalanyl, benzoimidazolyl, benzothiazolyl, benzoxazolyl, 5 benzofuranyl, benzothiophenyl, indolyl, isoindolyl, 1H-indazolyl, quinazolinyl, phthalazinyl and the like.

As used herein, an example of (ethyl)(ethoxy)pyridyl includes 3-ethoxy-4-ethyl-2-pyridyl, 4-ethoxy-3-ethyl-2-pyridyl and the like.

- As used herein, an example of (chloro)(ethyl)pyridyl includes 3-chloro-4-ethyl-2-pyridyl, 4-chloro-3-ethyl-2-pyridyl and the like.

As used herein, an example of (fluoro)(ethyl)phenyl includes 3-fluoro-4-ethyl-2-pyridyl, 4-fluoro-3-ethyl-2-pyridyl and the like.

- Preferred compounds of this invention are those of the formula (I) wherein Z is OH, C<sub>1-6</sub> alkoxy, dimethylamino, methylamino, amino, N-methoxy-N-methylamino, 2-cyanoethylamino, 2-hydroxyethylamino, pyrrolidinyl, piperidino, 15 piperazinyl, N-methyl-piperazinyl, morpholino, methoxyamino, piperazinyl, aminopyrrolidinyl or aminoethylamino.

Further preferred compounds of this invention are those of the formula (I) wherein

- 20 Z is OH or C<sub>1-6</sub> alkoxy; and

Q is selected from the following:

- (a) phenyl optionally substituted with one, two or three substituents independently selected from
- (a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-25 substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>R<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl,
- 30 (a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally substituted with one, two or three substituents independently

- selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
- 5 (a-3) 5-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
- 10 (a-4) 6-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
- 15 (b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),
- 20 (c) a 5-membered monocyclic aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);
- 25 (d) C<sub>3-7</sub> cycloalkyl selected from cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl, and the said cycloalkyl being optionally substituted with one substituent selected from OH, methyl, ethyl, propyl, F, Cl and CF<sub>3</sub>; and
- (e) a benzo-fuzed heterocycle selected from quinolyl, isoquinolyl, cinnolinyl, quinoxaliny, benzoimidazolyl, benzothiazolyl, benzoxazolyl, benzofuranyl, benzothiophenyl and indolyl, and the benzo-fuzed heterocycle being optionally substituted with one, two, or three substituents independently selected from the group (a-1).
- 30

Further preferred compounds of this invention are those of the formula (I) wherein

**Q** is selected from the following:

- 5 (a) phenyl optionally substituted with one, two or three substituents independently selected from

10 (a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>R<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl,

15 (a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

20 (a-3) 5-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

25 (a-4) 6-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

30 (b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),

(c) a 5-membered monocyclic aromatic group containing one heteroatom

selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);

- 5 (d) cyclopropyl, cyclobutyl and cyclohexyl; and  
(e) quinolyl or isoquinolyl, and said quinolyl or isoquinolyl being optionally substituted with one substituent selected from the group halo, C<sub>1-4</sub> alkyl, NH<sub>2</sub>, OH, C<sub>1-4</sub> alkoxy and C<sub>1-4</sub> halo-substituted alkyl.

10 Further preferred compounds of this invention are those of the formula (I)  
wherein

Z is OH, C<sub>1-6</sub> alkoxy;

Q is selected from the following:

- 15 (a) phenyl optionally substituted with one, two or three substituents  
independently selected from  
(a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-  
substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub>  
alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub>  
alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>1</sup>R<sup>2</sup>, acetyl-  
-COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>1-4</sub>  
cycloalkyl,  
(a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally  
substituted with one, two or three substituents independently  
selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub>  
alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub>  
alkyl)amino, C<sub>1-4</sub> alkylamino and CN,  
(a-3) 5-membered monocyclic aromatic group optionally substituted with  
one, two or three substituents independently selected from halo, C<sub>1-4</sub>  
alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-  
substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub>  
alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

- (a-4) 6-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
- 5 (b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),
- 10 (c) a 5-membered monocyclic aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4); and
- 15 (e) isoquinolyl;

R<sup>1</sup> is hydrogen or C<sub>1-4</sub> alkyl;

R<sup>2</sup> and R<sup>3</sup> are independently H or methyl;

X is independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>NR<sup>3</sup>, acetyl, -COOR<sup>4</sup>, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl; and

n is 0, 1, 2, or 3.

25 Further preferred compounds of this invention are those of the formula (I) wherein

Z is OH, methoxy, ethoxy, n-propoxy, iso-propoxy, n-butoxy, iso-butoxy or tert-butoxy;

Q is selected from the following:

30 (a) phenyl optionally substituted with one or two substituents independently selected from

- (a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, -COOH, C<sub>1-4</sub> alkylsulfonylamino, nitro, C<sub>1-4</sub> alkylsulfonyl and cyano,
- 5 (a-2) phenyl or benzyloxy, and the phenyl or phenyl moiety of benzyloxy being optionally substituted with one substituent selected from C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, halo, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy and NH<sub>2</sub>,
- 10 (a-3) 5-membered monocyclic aromatic group selected from imidazolyl, thiazolyl, furyl, thienyl, pyrrolyl, tetrazolyl, triazolyl, oxazolyl, isoxazolyl, thiadiazolyl and pyrazolyl, and the 5-membered monocyclic aromatic group optionally being substituted with one substituent selected from C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, halo, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy and NH<sub>2</sub>.
- 15 (a-4) 6-membered monocyclic aromatic group selected from pyridyl, pyrazinyl, pyrimidinyl and pyridazinyl, and the 6-membered monocyclic aromatic group optionally being substituted with one substituent selected from C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, halo, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy and NH<sub>2</sub>.
- 20 (b) a 6-membered monocyclic aromatic group selected from pyridyl, pyrazinyl, pyrimidinyl and pyridazinyl, and said monocyclic aromatic group being optionally substituted with one or two substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4).
- (c) a 5-membered monocyclic aromatic group selected from imidazolyl, thiazolyl, furyl, thienyl, pyrrolyl, tetrazolyl, triazolyl, oxazolyl, isoxazolyl, thiadiazolyl and pyrazolyl, and said monocyclic aromatic group being optionally substituted with one or two substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);
- 25 R<sup>1</sup> is hydrogen, methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl or tert-butyl;
- 30 X is independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino.

$C_{1-4}$  alkylamino, CN, HO-( $C_{1-4}$ ) alkyl,  $C_{1-4}$  alkoxy- $C_{1-4}$  alkyl,  $C_{1-4}$  alkylsulfonyl and aminosulfonyl; and

$n$  is 0, 1, 2, or 3.

Further preferred compounds of this invention are those of the formula (I)  
5 wherein

$Z$  is OH, methoxy, ethoxy, n-propoxy, iso-propoxy, n-butoxy, iso-butoxy or tert-butoxy;

$Q$  is selected from the following:

- (a) phenyl optionally substituted with one or two substituents independently selected from  
10 (a-1) fluoro, chloro, bromo, iodo, methyl, ethyl, propyl, butyl,  $CH_2F$ ,  $CHF_2$ ,  $CF_3$ , methoxy, ethoxy, n-propoxy, n-butoxy, isopropoxy,  $CH_2F-O-$ ,  $CHF_2-O-$ ,  $CF_3-O-$ , methylthio, ethylthio, hydroxymethyl, methoxymethyl, methoxyethyl, ethoxymethyl, hydroxy, nitro, methylsulfonyl, cyano,  $(HO)(H_3C)_2C-$ , acetyl and methylsulfonylamino,  
15 (a-2) phenyl or benzyloxy, and the phenyl or phenyl moiety of benzyloxy being optionally substituted with one substituent selected from methyl, ethyl, propyl,  $CF_3$ , F, Cl, OH, methoxy, ethoxy and  $NH_2$ ,  
20 (a-3) 5-membered monocyclic aromatic group selected from furyl, thienyl and pyrrolyl, and the 5-membered monocyclic aromatic group optionally being substituted with one substituent selected from methyl, ethyl, propyl,  $CF_3$ , F, Cl, OH, methoxy, ethoxy and  $NH_2$ ,  
25 (a-4) pyridyl optionally substituted with one substituent selected from methyl, ethyl, propyl,  $CF_3$ , F, Cl, OH, methoxy, ethoxy and  $NH_2$ ;  
(b) pyridyl optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-1), (a-2), (a-3) and (a-4),  
30 (c) imidazolyl, thiazolyl, furyl, thienyl, isoxazolyl, 1,2,3-thiadiazolyl or pyrrolyl, and said imidazolyl, thiazolyl, furyl, thienyl, isoxazolyl, 1,2,3-thiadiazolyl or pyrrolyl being optionally substituted with one or two

substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);

**R<sup>1</sup>** is hydrogen, methyl, ethyl, n-propyl, iso-propyl;

**X** is independently selected from fluoro, chloro, bromo, methyl, ethyl, propyl, butyl,

5 CH<sub>2</sub>F, CHF<sub>2</sub>, CF<sub>3</sub>, methoxy, CF<sub>3</sub>O or ethoxy; and

**n** is 0, 1 or 2.

Further preferred compounds of this invention are those of the formula (I) wherein

- 10 **Z** is OH, ethoxy or methoxy; **Q** is phenyl, chlorophenyl, fluorophenyl, bromophenyl, methylphenyl, methoxyphenyl, (furyl)phenyl, trifluoromethylphenyl, trifluoromethoxyphenyl, pyridyl, methylpyridyl, ethylpyridyl, propylpyridyl, dimethylpyridyl, chloropyridyl, fluoropyridyl, trifluoromethylpyridyl, methoxypyridyl, (ethyl)(ethoxy)pyridyl, (chloro)(ethyl)pyridyl, thiazolyl, methylthiazolyl, furyl, methoxymethylfuryl, isoquinolyl, cyclohexyl, methoxyphenyl, (fluoro)(ethyl)pyridyl,
- 15 dimethylpyridyl or (ethoxy)(ethyl)pyridyl;

**R<sup>1</sup>** is hydrogen; **X** is fluoro, chloro, methyl, ethyl, isopropyl, tert-butyl, CF<sub>3</sub> or methoxy; and **n** is 1 or 2.

Further preferred compounds of this invention are those of the formula (I) wherein

- 20 **Z** is OH, ethoxy or methoxy; **Q** is phenyl, chlorophenyl, pyridyl, methylpyridyl, ethylpyridyl, propylpyridyl or chloropyridyl; **R<sup>1</sup>** is hydrogen; **X** is fluoro, chloro, methyl or CF<sub>3</sub>; and **n** is 1 or 2.

Preferred individual compounds of this invention are:

- ethyl (2-benzoyl-6-chloro-1H-indol-3-yl)acetate;
- 25 (2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid;
- (2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid, sodium salt;
- [6-chloro-2-(2-methylbenzoyl)-1H-indol-3-yl]acetic acid;
- [6-chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid;
- [6-chloro-2-(4-methylbenzoyl)-1H-indol-3-yl]acetic acid;
- 30 [6-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;
- methyl [6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetate;

- [6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-fluorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-fluorobenzoyl)-1H-indol-3-yl]acetic acid;  
[2-(3-bromobenzoyl)-6-chloro-1H-indol-3-yl]acetic acid;
- 5 [2-(4-bromobenzoyl)-6-chloro-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-trifluoromethylbenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-trifluoromethylbenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3,4-dichlorobenzoyl)-1H-indol-3-yl]acetic acid;  
(2-benzoyl-4-chloro-1H-indol-3-yl)acetic acid;
- 10 [5-chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
[2-(3-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;
- 15 [5-methoxy-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
(2-benzoyl-7-chloro-1H-indol-3-yl)acetic acid;  
(2-benzoyl-4,5-dichloro-1H-indol-3-yl)acetic acid;  
(2-benzoyl-4,6-dichloro-1H-indol-3-yl)acetic acid;  
(2-benzoyl-5,6-dichloro-1H-indol-3-yl)acetic acid;
- 20 *dl*-2-(2-benzoyl-6-chloro-1H-indol-3-yl)propanoic acid;  
less polar antipode, 2-(2-benzoyl-6-chloro-1H-indol-3-yl)propanoic acid;  
more polar antipode, 2-(2-benzoyl-6-chloro-1H-indol-3-yl)propanoic acid;  
[6-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 25 methyl [6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(pyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 30 [5-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;

- methyl [5-chloro-2-(thiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(thiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl (2-benzoyl-6-chloro-1H-indol-3-yl)acetate;  
(2-benzoyl-6-chloro-1H-indol-3-yl)-N,N-dimethylacetamide;
- 5 (2-benzoyl-6-chloro-1H-indol-3-yl)-N-methylacetamide;  
(2-benzoyl-6-chloro-1H-indol-3-yl)acetamide;  
(2-benzoyl-6-chloro-1H-indol-3-yl)-N-methoxy-N-methylacetamide;  
2-(2-benzoyl-6-chloro-1H-indol-3-yl)-1-piperidino-1-ethanone;  
2-(2-benzoyl-6-chloro-1H-indol-3-yl)-1-(4-methyl-1-piperazinyl)-1-ethanone;
- 10 (2-benzoyl-6-chloro-1H-indol-3-yl)-N-(2-cyanoethyl)acetamide;  
(2-benzoyl-6-chloro-1H-indol-3-yl)-N-(2-hydroxyethyl)acetamide;  
2-(2-benzoyl-6-chloro-1H-indol-3-yl)-1-morpholino-1-ethanone;  
[2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(2-furylcarbonyl)-1H-indol-3-yl]acetic acid;
- 15 [6-chloro-2-(cyclohexanecarbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 20 methyl [5-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 25 [5-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 30 methyl [2-(4-*tert*-butylpyridine-2-carbonyl)-6-chloro-1H-indol-3-yl]acetate;  
[2-(4-*tert*-butylpyridine-2-carbonyl)-6-chloro-1H-indol-3-yl]acetic acid;

- methyl [2-(4-*tert*-butylpyridine-2-carbonyl)-5-chloro-1H-indol-3-yl]acetate;  
[2-(4-*tert*-butylpyridine-2-carbonyl)-5-chloro-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(3-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(3-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 5   methyl [5-chloro-2-(3-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(3-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 10   [5-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;  
[5-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;
- 15   methyl [5-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 20   [5-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(pyridine-3-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(pyridine-3-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(pyridine-4-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(pyridine-4-carbonyl)-1H-indol-3-yl]acetic acid;
- 25   methyl [6-chloro-2-[4-(hydroxymethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[4-(hydroxymethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-[4-(hydroxymethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;  
[5-chloro-2-[4-(hydroxymethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(3,4-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 30   [5-chloro-2-(3,4-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;

- [5-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 5 [6-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(3,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(3,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 10 methyl [5-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(3-ethoxy-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 15 [6-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 20 methyl [6-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5,6-dichloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5,6-dichloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 25 [5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 30 methyl [6-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;

- methyl [5-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-ethyl-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-ethyl-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 5   methyl [6-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-isopropyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-isopropyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [2-(4-methylpyridine-2-carbonyl)-6-trifluoromethyl-1H-indol-3-yl]acetate;
- 10   [2-(4-methylpyridine-2-carbonyl)-6-trifluoromethyl-1H-indol-3-yl]acetic acid;  
methyl [5-*tert*-butyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-*tert*-butyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [2-(4-methylpyridine-2-carbonyl)-5-trifluoromethoxy-1H-indol-3-yl]acetate;  
[2-(4-methyl-2-pyridine-2-carbonyl)-5-trifluoromethoxy-1H-indol-3-yl]acetic acid;
- 15   methyl [2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethoxy-1H-indol-3-yl]acetate;  
[2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethoxy-1H-indol-3-yl]acetic acid;  
methyl [6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [2-(4-methylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetate;
- 20   [2-(4-methylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
methyl [2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetate;  
[2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
methyl (2-benzoyl-1H-indol-3-yl)acetate;  
(2-benzoyl-1H-indol-3-yl)acetic acid;
- 25   methyl [2-(4-chlorobenzoyl)-6-methyl-1H-indol-3-yl]acetate;  
[2-(4-chlorobenzoyl)-6-methyl-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-methyl-1H-indol-3-yl]acetic acid;  
methyl [6-methoxy-2-(4-chlorobenzoyl)-1H-indol-3-yl] acetate;  
[6-methoxy-2-(4-chlorobenzoyl)-1H-indol-3-yl] acetic acid;
- 30   [2-(4-chlorobenzoyl)-6-trifluoromethyl-1H-indol-3-yl]acetic acid;  
methyl [2-(4-chlorobenzoyl)-5-ethyl-1H-indol-3-yl]acetate;

- [2-(4-chlorobenzoyl)-5-ethyl-1H-indol-3-yl]acetic acid;  
methyl [2-(4-chlorobenzoyl)-5-methoxy-1H-indol-3-yl]acetate;  
[2-(4-chlorobenzoyl)-5-methoxy-1H-indol-3-yl]acetic acid;  
methyl [2-(4-chlorobenzoyl)-5-isopropyl-1H-indol-3-yl]acetate;
- 5 [2-(4-chlorobenzoyl)-5-isopropyl-1H-indol-3-yl]acetic acid;  
methyl [2-(4-chlorobenzoyl)-5-trifluoromethyl-1H-indol-3-yl]acetate;  
[2-(4-chlorobenzoyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
methyl [2-(4-chlorobenzoyl)-5-trifluoromethoxy-1H-indol-3-yl] acetate;  
[2-(4-chlorobenzoyl)-5-trifluoromethoxy-1H-indol-3-yl]acetic acid;
- 10 methyl [6-chloro-2-(2-methoxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(2-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(3-methoxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(3-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(3-benzyloxybenzoyl)-1H-indol-3-yl]acetate;
- 15 [6-chloro-2-(3-benzyloxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(3-hydroxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(3-hydroxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-benzoxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-benzyloxybenzoyl)-1H-indol-3-yl]acetic acid;
- 20 methyl [6-chloro-2-(4-hydroxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-hydroxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-isopropoxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-isopropoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-phenylbenzoyl)-1H-indol-3-yl]acetate;
- 25 [6-chloro-2-(4-phenylbenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;
- 30 methyl [5-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;

- methyl [6-chloro-2-(4-nitrobenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-nitrobenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[(4-methylsulfonyl)benzoyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[(4-methylsulfonyl)benzoyl]-1H-indol-3-yl]acetic acid;
- 5   methyl [6-chloro-2-[4-(methylsulfonylamino)benzoyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[4-(methylsulfonylamino)benzoyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(2-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(2,4-dichlorobenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-chloro-3-fluorobenzoyl)-1H-indol-3-yl]acetate;
- 10   [6-chloro-2-(4-chloro-3-fluorobenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-cyanobenzoyl)-1H-indol-3-yl]acetate;  
methyl [6-chloro-2-[4-bromobenzoyl]-1H-indol-3-yl]acetate;  
methyl [6-chloro-2-[4-(2-thienyl)benzoyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[4-(2-thienyl)benzoyl]-1H-indol-3-yl]acetic acid;
- 15   methyl [6-chloro-2-[4-(2-furyl)benzoyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[4-(2-furyl)benzoyl]-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[4-(3-pyridyl)benzoyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[4-(3-pyridyl)benzoyl]-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[4-(2-thiazolyl)benzoyl]-1H-indol-3-yl]acetate;
- 20   [6-chloro-2-[4-(2-thiazolyl)benzoyl]-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(3-bromobenzoyl)-1H-indol-3-yl]acetate;  
methyl [6-chloro-2-[3-(2-furyl)benzoyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[3-(2-furyl)benzoyl]-1H-indol-3-yl]acetic acid;  
methyl *dl*-2-[6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]propionate;
- 25   *dl*-2-[2-(4-chlorobenzoyl)-6-chloro-1H-indol-3-yl]propionic acid;  
methyl [5-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;
- 30   methyl [5-chloro-2-(5-methylisoxazole-3-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(5-methylisoxazole-3-carbonyl)-1H-indol-3-yl]acetic acid;

- methyl [6-chloro-2-(5-methylisoxazole-3-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(5-methylisoxazole-3-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-methyl-1,2,3-thiadiazole-5-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-methyl-1,2,3-thiadiazole-5-carbonyl)-1H-indol-3-yl]acetic acid;
- 5   methyl [6-chloro-2-(4-methyl-1,2,3-thiadiazole-5-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-methyl-1,2,3-thiadiazole-5-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate;
- 10   [6-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(2-thienyl)carbonylindol-3-yl]acetic acid;  
methyl [6-chloro-2-[3-(1-hydroxy-1-methylethyl)-2-furoyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[3-(1-hydroxy-1-methylethyl)-2-furoyl]-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[3-methoxymethyl-2-furoyl]-1H-indol-3-yl]acetate;
- 15   [6-chloro-2-[3-methoxymethyl-2-furoyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetate;  
methyl [5-chloro-2-(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 20   methyl [5-chloro-2-(imidazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(imidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(imidazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(imidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate;
- 25   [5-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(1-methylpyrrole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(1-methylpyrrole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(2-methylimidazole-4-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(2-methylimidazole-4-carbonyl)-1H-indol-3-yl]acetic acid;
- 30   methyl [5-chloro-2-(thiazole-5-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(thiazole-5-carbonyl)-1H-indol-3-yl]acetic acid;

- methyl [6-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-[3-(ethoxycaronyl)isoxazole-5-carbonyl]-1H-indol-3-yl]acetate;  
[5-chloro-2-[3-(carboxy)isoxazole-5-carbonyl]-1H-indol-3-yl]acetic acid;
- 5   methyl [6-chloro-2-cyclopropanecarbonyl-1H-indol-3-yl]acetate;  
[6-chloro-2-cyclopropanecarbonyl-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-cyclobutanecarbonyl-1H-indol-3-yl]acetate;  
[6-chloro-2-cyclobutanecarbonyl-1H-indol-3-yl]acetic acid;  
methyl [5-(*tert*-butyl)-2-(4-chlorobenzoyl)-1H-indol-3-yl] acetate;
- 10   [5-(*tert*-butyl)-2-(4-chlorobenzoyl)-1H-indol-3-yl] acetic acid;  
[6-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]-*N,N*-dimethylacetamide;  
[6-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]-*N*-methylacetamide;  
[5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]-*N*-(2-hydroxyethyl)acetamide;
- 15   [5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]-*N*-methoxyacetamide;  
2-[5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]-1-piperazinyl-1-ethanone;  
[5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]-*N*-(2-aminoethyl)acetamide;  
2-[5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]-1-(3-amino-1-pyrrolidinyl)  
)-1-ethanone;
- 20   [6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;
- 25   [6-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(2-nitrobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(2,4-dimethoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-difluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(2,5-dimethoxybenzoyl)-1H-indol-3-yl]acetic acid;
- 30   methyl [5-acetyl-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetate;  
[5-acetyl-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;

- methyl [6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetate;  
methyl [6-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-fluoro-2-(4-chlorobenzoyl)-1H-indol-3-yl] acetate;
- 5 [6-fluoro-2-(4-chlorobenzoyl) -1H-indol-3-yl]acetic acid;  
[2-(4-methylpyridine-2-carbonyl)-5-methylthio-1H-indol-3-yl]acetic acid;  
[2-(4-methylpyridine-2-carbonyl)-5-methylthio-1H-indol-3-yl]acetic acid, and a salt thereof.

Preferred individual compounds of this invention are:

- 10 ethyl (2-benzoyl-6-chloro-1H-indol-3-yl)acetate;  
(2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid;  
(2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid, sodium salt;  
[6-chloro-2-(2-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid;
- 15 [6-chloro-2-(4-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-fluorobenzoyl)-1H-indol-3-yl]acetic acid;
- 20 [6-chloro-2-(4-fluorobenzoyl)-1H-indol-3-yl]acetic acid;  
[2-(3-bromobenzoyl)-6-chloro-1H-indol-3-yl]acetic acid;  
[2-(4-bromobenzoyl)-6-chloro-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-trifluoromethylbenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-trifluoromethylbenzoyl)-1H-indol-3-yl]acetic acid;
- 25 [6-chloro-2-(3,4-dichlorobenzoyl)-1H-indol-3-yl]acetic acid;  
(2-benzoyl-4-chloro-1H-indol-3-yl)acetic acid;  
[5-chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;
- 30 [2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
[2-(3-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;

- [5-methoxy-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
(2-benzoyl-7-chloro-1H-indol-3-yl)acetic acid;  
(2-benzoyl-4,5-dichloro-1H-indol-3-yl)acetic acid;  
(2-benzoyl-4,6-dichloro-1H-indol-3-yl)acetic acid;
- 5 (2-benzoyl-5,6-dichloro-1H-indol-3-yl)acetic acid;  
*dl*-2-(2-benzoyl-6-chloro-1H-indol-3-yl)propanoic acid;  
less polar antipode, 2-(2-benzoyl-6-chloro-1H-indol-3-yl)propanoic acid;  
more polar antipode, 2-(2-benzoyl-6-chloro-1H-indol-3-yl)propanoic acid;  
[6-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 10 [6-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(pyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 15 methyl [5-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(thiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(thiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 20 methyl (2-benzoyl-6-chloro-1H-indol-3-yl)acetate;  
[2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(2-furylcarbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(cyclohexanecarbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetate;
- 25 [6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 30 [5-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;

- [5-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[2-(4-*tert*-butylpyridine-2-carbonyl)-6-chloro-1H-indol-3-yl]acetic acid;  
[2-(4-*tert*-butylpyridine-2-carbonyl)-5-chloro-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 5 [5-chloro-2-(3-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
[5-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;
- 10 [5-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(pyridine-3-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(pyridine-4-carbonyl)-1H-indol-3-yl]acetic acid;
- 15 [6-chloro-2-[4-(hydroxymethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
[5-chloro-2-[4-(hydroxymethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(3,4-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 20 [6-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-ethoxy-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 25 [6-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5,6-dichloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 30 [5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;

- [5-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-ethyl-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 5 [6-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-isopropyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[2-(4-methylpyridine-2-carbonyl)-6-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[5-*tert*-butyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[2-(4-methyl-2-pyridine-2-carbonyl)-5-trifluoromethoxy-1H-indol-3-yl]acetic acid;
- 10 [2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethoxy-1H-indol-3-yl]acetic acid;  
[6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[2-(4-methylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
(2-benzoyl-1H-indol-3-yl)acetic acid;
- 15 [2-(4-chlorobenzoyl)-6-methyl-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-methyl-1H-indol-3-yl]acetic acid;  
[6-methoxy-2-(4-chlorobenzoyl)-1H-indol-3-yl] acetic acid;  
[2-(4-chlorobenzoyl)-6-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-ethyl-1H-indol-3-yl]acetic acid;
- 20 [2-(4-chlorobenzoyl)-5-methoxy-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-isopropyl-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-trifluoromethoxy-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(2-methoxybenzoyl)-1H-indol-3-yl]acetic acid;
- 25 [6-chloro-2-(3-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-benzyloxybenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-hydroxybenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-benzyloxybenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-hydroxybenzoyl)-1H-indol-3-yl]acetic acid;
- 30 [6-chloro-2-(4-isopropoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-phenylbenzoyl)-1H-indol-3-yl]acetic acid;

- [6-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-nitrobenzoyl)-1H-indol-3-yl]acetic acid;
- 5 [6-chloro-2-[(4-methylsulfonyl)benzoyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-[4-(methylsulfonylamino)benzoyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(2-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(2,4-dichlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-chloro-3-fluorobenzoyl)-1H-indol-3-yl]acetic acid;
- 10 methyl [6-chloro-2-(4-cyanobenzoyl)-1H-indol-3-yl]acetate;  
methyl [6-chloro-2-[4-bromobenzoyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[4-(2-thienyl)benzoyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-[4-(2-furyl)benzoyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-[4-(3-pyridyl)benzoyl]-1H-indol-3-yl]acetic acid;
- 15 [6-chloro-2-[4-(2-thiazolyl)benzoyl]-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(3-bromobenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-[3-(2-furyl)benzoyl]-1H-indol-3-yl]acetic acid;  
*dl*-2-[2-(4-chlorobenzoyl)-6-chloro-1H-indol-3-yl]propionic acid;  
[5-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;
- 20 [6-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(5-methylisoxazole-3-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(5-methylisoxazole-3-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methyl-1,2,3-thiadiazole-5-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-methyl-1,2,3-thiadiazole-5-carbonyl)-1H-indol-3-yl]acetic acid;
- 25 [5-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(2-thienyl)carbonylindol-3-yl]acetic acid;  
[6-chloro-2-[3-(1-hydroxy-1-methylethyl)-2-furoyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-[3-methoxymethyl-2-furoyl]-1H-indol-3-yl]acetic acid;
- 30 [6-chloro-2-(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetate;

- [5-cloro-2(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-cloro-2-(imidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-cloro-2-(imidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 5 [5-chloro-2-(1-methylpyrrole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(2-methylimidazole-4-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(thiazole-5-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-[3-(carboxy)isoxazole-5-carbonyl]-1H-indol-3-yl]acetic acid;
- 10 [6-chloro-2-cyclopropanecarbonyl-1H-indol-3-yl]acetic acid;  
[6-chloro-2-cyclobutanecarbonyl-1H-indol-3-yl]acetic acid;  
[5-(*tert*-butyl)-2-(4-chlorobenzoyl)-1H-indol-3-yl] acetic acid;  
[6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
[6-chloro-5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 15 methyl [6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-ethyl-3-fluoro-pyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(2-nitrobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(2,4-dimethoxybenzoyl)-1H-indol-3-yl]acetic acid;
- 20 [6-chloro-2-(4-difluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(2,5-dimethoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[5-acetyl-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid, and a salt thereof.

Preferred individual compounds of this invention are:

- ethyl (2-benzoyl-6-chloro-1H-indol-3-yl)acetate;
- 25 (2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid;  
[6-chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetate;
- 30 [6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-fluorobenzoyl)-1H-indol-3-yl]acetic acid;

- [6-chloro-2-(4-fluorobenzoyl)-1H-indol-3-yl]acetic acid;  
[2-(3-bromobenzoyl)-6-chloro-1H-indol-3-yl]acetic acid;  
[2-(4-bromobenzoyl)-6-chloro-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-trifluoromethylbenzoyl)-1H-indol-3-yl]acetic acid;
- 5 [6-chloro-2-(4-trifluoromethylbenzoyl)-1H-indol-3-yl]acetic acid;  
(2-benzoyl-4-chloro-1H-indol-3-yl)acetic acid;  
[5-chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;
- 10 [2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
[2-(3-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
(2-benzoyl-4,5-dichloro-1H-indol-3-yl)acetic acid;  
(2-benzoyl-4,6-dichloro-1H-indol-3-yl)acetic acid;  
(2-benzoyl-5,6-dichloro-1H-indol-3-yl)acetic acid;
- 15 *dl*-2-(2-benzoyl-6-chloro-1H-indol-3-yl)propanoic acid;  
less polar antipode, 2-(2-benzoyl-6-chloro-1H-indol-3-yl)propanoic acid;  
more polar antipode, 2-(2-benzoyl-6-chloro-1H-indol-3-yl)propanoic acid;  
[6-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 20 methyl [6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(pyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 25 [5-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(thiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(thiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl (2-benzoyl-6-chloro-1H-indol-3-yl)acetate;
- 30 [6-chloro-2-(2-furylcarbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(cyclohexanecarbonyl)-1H-indol-3-yl]acetic acid;

- methyl [6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 5   methyl [5-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 10   [6-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [2-(4-*tert*-butylpyridine-2-carbonyl)-6-chloro-1H-indol-3-yl]acetate;  
[2-(4-*tert*-butylpyridine-2-carbonyl)-6-chloro-1H-indol-3-yl]acetic acid;
- 15   methyl [6-chloro-2-(3-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(3-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 20   [5-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;  
[5-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;
- 25   methyl [5-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 30   [5-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-[4-(hydroxymethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;

- [5-chloro-2-[4-(hydroxymethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 5 [6-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 10 methyl [6-chloro-2-(3,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(3,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 15 [6-chloro-2-(3-ethoxy-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 20 methyl [5-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5,6-dichloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 25 [5,6-dichloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 30 methyl [5-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;

- methyl [6-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 5   methyl [5-ethyl-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-ethyl-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-isopropyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 10   [5-isopropyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [2-(4-methylpyridine-2-carbonyl)-6-trifluoromethyl-1H-indol-3-yl]acetate;  
[2-(4-methylpyridine-2-carbonyl)-6-trifluoromethyl-1H-indol-3-yl]acetic acid;  
methyl [5-*tert*-butyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-*tert*-butyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 15   methyl [2-(4-methylpyridine-2-carbonyl)-5-trifluoromethoxy-1H-indol-3-yl]acetate;  
[2-(4-methyl-2-pyridine-2-carbonyl)-5-trifluoromethoxy-1H-indol-3-yl]acetic acid;  
methyl [6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [2-(4-methylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetate;
- 20   [2-(4-methylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
methyl [2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetate;  
[2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
methyl [2-(4-chlorobenzoyl)-6-methyl-1H-indol-3-yl]acetate;  
[2-(4-chlorobenzoyl)-6-methyl-1H-indol-3-yl]acetic acid;
- 25   [2-(4-chlorobenzoyl)-5-methyl-1H-indol-3-yl]acetic acid;  
methyl [2-(4-chlorobenzoyl)-5-trifluoromethyl-1H-indol-3-yl]acetate;  
[2-(4-chlorobenzoyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
methyl [2-(4-chlorobenzoyl)-5-trifluoromethoxy-1H-indol-3-yl] acetate;  
[2-(4-chlorobenzoyl)-5-trifluoromethoxy-1H-indol-3-yl]acetic acid;
- 30   methyl [6-chloro-2-(3-methoxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(3-methoxybenzoyl)-1H-indol-3-yl]acetic acid;

- methyl [6-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;
- 5   methyl [5-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[4-(2-furyl)benzoyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[4-(2-furyl)benzoyl]-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetate;
- 10   [5-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(5-methylisoxazole-3-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(5-methylisoxazole-3-carbonyl)-1H-indol-3-yl]acetic acid;
- 15   methyl [5-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[3-methoxymethyl-2-furoyl]-1H-indol-3-yl]acetate;
- 20   [6-chloro-2-[3-methoxymethyl-2-furoyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetate;  
methyl [5-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(2-methylimidazole-4-carbonyl)-1H-indol-3-yl]acetate;
- 25   [5-chloro-2-(2-methylimidazole-4-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;
- 30   [6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;

methyl [6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetate, and a salt thereof.

Preferred individual compounds of this invention are:

- ethyl (2-benzoyl-6-chloro-1H-indol-3-yl)acetate;  
(2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid;
- 5 [6-chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;
- 10 [6-chloro-2-(3-fluorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-fluorobenzoyl)-1H-indol-3-yl]acetic acid;  
[2-(3-bromobenzoyl)-6-chloro-1H-indol-3-yl]acetic acid;  
[2-(4-bromobenzoyl)-6-chloro-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-trifluoromethylbenzoyl)-1H-indol-3-yl]acetic acid;
- 15 [6-chloro-2-(4-trifluoromethylbenzoyl)-1H-indol-3-yl]acetic acid;  
(2-benzoyl-4-chloro-1H-indol-3-yl)acetic acid;  
[5-chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;
- 20 [2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
[2-(3-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
(2-benzoyl-4,5-dichloro-1H-indol-3-yl)acetic acid;  
(2-benzoyl-4,6-dichloro-1H-indol-3-yl)acetic acid;  
(2-benzoyl-5,6-dichloro-1H-indol-3-yl)acetic acid;
- 25 *dl*-2-(2-benzoyl-6-chloro-1H-indol-3-yl)propanoic acid;  
less polar antipode, 2-(2-benzoyl-6-chloro-1H-indol-3-yl)propanoic acid;  
more polar antipode, 2-(2-benzoyl-6-chloro-1H-indol-3-yl)propanoic acid;  
[6-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 30 methyl [6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;

- [6-chloro-2-(pyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 5 [6-chloro-2-(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(thiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(thiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl (2-benzoyl-6-chloro-1H-indol-3-yl)acetate;  
[6-chloro-2-(2-furylcarbonyl)-1H-indol-3-yl]acetic acid;
- 10 [6-chloro-2-(cyclohexanecarbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 15 [5-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[2-(4-*tert*-butylpyridine-2-carbonyl)-6-chloro-1H-indol-3-yl]acetic acid;
- 20 [6-chloro-2-(3-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
[5-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;
- 25 [5-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-[4-(hydroxymethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 30 [6-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;

- [5-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-ethoxy-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
5 [6-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5,6-dichloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
10 [5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
15 [5-ethyl-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-isopropyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[2-(4-methylpyridine-2-carbonyl)-6-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[5-*tert*-butyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
20 [2-(4-methyl-2-pyridine-2-carbonyl)-5-trifluoromethoxy-1H-indol-3-yl]acetic acid;  
[6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[2-(4-methylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-6-methyl-1H-indol-3-yl]acetic acid;  
25 [2-(4-chlorobenzoyl)-5-methyl-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-trifluoromethoxy-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;  
30 [5-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;

- [6-chloro-2-[4-(2-furyl)benzoyl]-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(5-methylisoxazole-3-carbonyl)-1H-indol-3-yl]acetic acid;  
5 [5-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-[3-methoxymethyl-2-furoyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
10 [5-chloro-2-(2-methylimidazole-4-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
15 2-[6-chloro-2-[(4-ethyl-3-fluoro-2-pyridinyl)carbonyl]-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetate, and a salt thereof.

Preferred individual compounds of this invention are:

- (2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid;  
[6-chloro-2-(4-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
20 [6-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-fluorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-fluorobenzoyl)-1H-indol-3-yl]acetic acid;  
25 [2-(3-bromobenzoyl)-6-chloro-1H-indol-3-yl]acetic acid;  
[2-(4-bromobenzoyl)-6-chloro-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-trifluoromethylbenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
30 [5-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;

- [2-(3-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
(2-benzoyl-4,5-dichloro-1H-indol-3-yl)acetic acid;  
(2-benzoyl-4,6-dichloro-1H-indol-3-yl)acetic acid;  
(2-benzoyl-5,6-dichloro-1H-indol-3-yl)acetic acid;
- 5 [6-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(pyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 10 [5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(thiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(thiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 15 methyl (2-benzoyl-6-chloro-1H-indol-3-yl)acetate;  
[6-chloro-2-(cyclohexanecarbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 20 [6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 25 methyl [6-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 30 [5-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;

- [6-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;  
[5-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 5 [5-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 10 methyl [5-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 15 [6-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(3-ethoxy-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 20 methyl [6-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 25 [6-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5,6-dichloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5,6-dichloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 30 methyl [5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;

- methyl [5-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-isopropyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-isopropyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 5   methyl [2-(4-methylpyridine-2-carbonyl)-6-trifluoromethyl-1H-indol-3-yl]acetate;  
[2-(4-methylpyridine-2-carbonyl)-6-trifluoromethyl-1H-indol-3-yl]acetic acid;  
methyl [5-*tert*-butyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-*tert*-butyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [2-(4-methylpyridine-2-carbonyl)-5-trifluoromethoxy-1H-indol-3-yl]acetate;
- 10   [2-(4-methyl-2-pyridine-2-carbonyl)-5-trifluoromethoxy-1H-indol-3-yl]acetic acid;  
methyl [6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [2-(4-methylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetate;  
[2-(4-methylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;
- 15   methyl [2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetate;  
[2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-methyl-1H-indol-3-yl]acetic acid;  
methyl [2-(4-chlorobenzoyl)-5-trifluoromethyl-1H-indol-3-yl]acetate;  
[2-(4-chlorobenzoyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;
- 20   methyl [6-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetate;
- 25   [5-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[4-(2-furyl)benzoyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[4-(2-furyl)benzoyl]-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;
- 30   methyl [6-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;

- methyl [5-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 5   methyl [6-chloro-2-[3-methoxymethyl-2-furoyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[3-methoxymethyl-2-furoyl]-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(2-methylimidazole-4-carbonyl)-1H-indol-3-yl]acetate;
- 10   [5-chloro-2-(2-methylimidazole-4-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 15   methyl [6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetate, and a salt thereof.

Preferred individual compounds of this invention are:

- (2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid;  
[6-chloro-2-(4-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;
- 20   methyl [6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-fluorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-fluorobenzoyl)-1H-indol-3-yl]acetic acid;  
[2-(3-bromobenzoyl)-6-chloro-1H-indol-3-yl]acetic acid;
- 25   [2-(4-bromobenzoyl)-6-chloro-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-trifluoromethylbenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;
- 30   [2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
[2-(3-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;

- (2-benzoyl-4,5-dichloro-1H-indol-3-yl)acetic acid;  
(2-benzoyl-4,6-dichloro-1H-indol-3-yl)acetic acid;  
(2-benzoyl-5,6-dichloro-1H-indol-3-yl)acetic acid;  
[6-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
5 [6-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(pyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
10 methyl [5-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(thiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(thiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl (2-benzoyl-6-chloro-1H-indol-3-yl)acetate;  
15 [6-chloro-2-(cyclohexanecarbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
20 [5-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
25 [6-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
[5-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
30 [5-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;

- [6-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-ethoxy-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 5 [5-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5,6-dichloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 10 [5-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-isopropyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[2-(4-methylpyridine-2-carbonyl)-6-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[5-*tert*-butyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[2-(4-methyl-2-pyridine-2-carbonyl)-5-trifluoromethoxy-1H-indol-3-yl]acetic acid;
- 15 [6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[2-(4-methylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;
- 20 [5-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-[4-(2-furyl)benzoyl]-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;
- 25 methyl [5-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-[3-methoxymethyl-2-furoyl]-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(2-methylimidazole-4-carbonyl)-1H-indol-3-yl]acetic acid;
- 30 [6-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;

- [6-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetate;  
[6-chloro-5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;  
5 [6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid,  
and a salt thereof.

Preferred individual compounds of this invention are:

- (2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid;  
[6-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
10 [6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
[2-benzoyl-5,6-dichloro-1H-indol-3-yl]acetic acid;  
15 [6-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(pyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
20 [5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
25 [6-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
30 methyl [2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetate;  
[2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;

- methyl [6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 5   methyl [6-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 10   [5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;
- 15   [6-chloro-5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 20   [6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;
- 25   [6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid (cj-020,099);  
methyl [6-chloro-5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate,  
and a salt thereof.

Most preferred individual compounds are:

- (2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid;
- 30   [6-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;

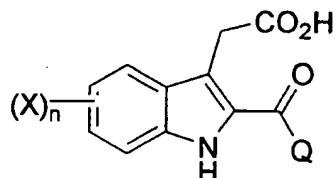
- [5-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
(2-benzoyl-5,6-dichloro-1H-indol-3-yl)acetic acid;
- 5 [6-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(pyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 10 [6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 15 [2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 20 [5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 25 [6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid,  
and a salt thereof.
- 30 Preferred pharmaceutical compositions of this invention comprise those compounds of the formula (I), wherein the compound is as defined above.

Most preferred individual compounds to be contained in the pharmaceutical compositions are:

- (2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid;  
[6-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;
- 5 [6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
(2-benzoyl-5,6-dichloro-1H-indol-3-yl)acetic acid;
- 10 [6-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(pyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 15 [6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 20 [2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 25 [5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 30 [6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;

[5-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid,  
and a salt thereof.

Also, the present invention provides a process for preparing a compound of the  
5 formula:



7-IV

Q is selected from the following:

- (a) phenyl optionally substituted with one, two or three substituents independently selected from
  - (a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>R<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl,
  - (a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
  - (a-3) 5-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
  - (a-4) 6-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-</sub>

$C_1-C_4$  alkyl, halo-substituted  $C_1-C_4$  alkyl, OH,  $C_1-C_4$  alkoxy, halo-substituted  $C_1-C_4$  alkoxy,  $C_1-C_4$  alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-( $C_1-C_4$  alkyl)amino,  $C_1-C_4$  alkylamino and CN,

- (b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),
- (c) a 5-membered monocyclic aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);
- (d)  $C_{3-7}$  cycloalkyl optionally substituted with one or two substituents independently selected from OH,  $C_1-C_4$  alkyl, halo and halo-substituted  $C_1-C_4$  alkyl; and
- (e) a benzo-fused heterocycle optionally substituted with one, two or three substituents independently selected from the group (a-1);

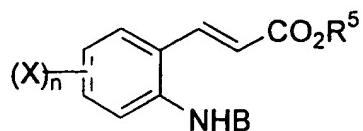
**R<sup>2</sup> and R<sup>3</sup>** are independently H, OH,  $C_1-C_4$  alkoxy,  $C_1-C_4$  alkyl or  $C_1-C_4$  alkyl substituted with halo, OH,  $C_1-C_4$  alkoxy, NH<sub>2</sub> or CN;

X is independently selected from halo,  $C_1-C_4$  alkyl, halo-substituted  $C_1-C_4$  alkyl, OH,  $C_1-C_4$  alkoxy, halo-substituted  $C_1-C_4$  alkoxy,  $C_1-C_4$  alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-( $C_1-C_4$  alkyl)amino,  $C_1-C_4$  alkylamino, CN, HO-( $C_1-C_4$ ) alkyl,  $C_1-C_4$  alkoxy- $C_1-C_4$  alkyl,  $C_1-C_4$  alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>NR<sup>3</sup>, acetyl, -COOH, -C(O)O- $C_1-C_4$  alkyl,  $C_1-C_4$  alkylsulfonylamino and  $C_{3-7}$  cycloalkyl; and

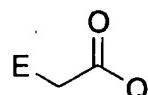
n is 0, 1, 2, 3 or 4,

which process comprises the steps of:

- i) reacting a compound of the formula:



wherein B is a suitable protecting group; R<sup>5</sup> is C<sub>1-6</sub> alkyl; X and n are as defined above, with a compound of the formula:



wherein E is halo and Q are as defined above, with a first base and a suitable solvent;

- ii) reacting the product of step i) with a second base.
- iii) reacting the product of step ii) with an acid.

Preferred process of the above mentioned process is a process, wherein said first base is potassium carbonate, potassium bicarbonate, sodium bicarbonate, sodium carbonate or cesium carbonate.

Preferred process of the above mentioned process is a process, wherein said first base is potassium carbonate.

Preferred process of the above mentioned process is a process, wherein said second base is aqueous sodium hydroxide, potassium hydroxide, sodium carbonate, potassium carbonate, sodium pentoxide (followed by water), sodium methoxide (followed by water) or potassium *t*-butoxide (followed by water).

Preferred process of the above mentioned process is a process, wherein said second base is sodium hydroxide.

Preferred process of the above mentioned process is a process, wherein said acid is aqueous hydrochloric acid, hydrobromic acid, sulfuric acid or ammonium chloride.

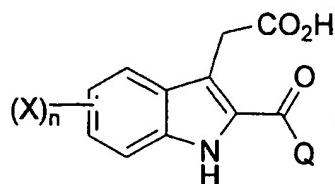
Preferred process of the above mentioned process is a process, wherein said acid is aqueous hydrochloric acid.

Preferred process of the above mentioned process is a process, wherein said solvent is *N,N*-dimethylacetamide, *N,N*-dimethylformamide, methyl ethyl ketone, acetone, or tetrahydrofuran.

Preferred process of the above mentioned process is a process, wherein said

solvent is *N,N*-dimethylacetamide.

Also, the present invention provides a process for preparing a compound of the formula:



#### 7-IV

5 wherein

**Q** is selected from the following:

- (a) phenyl optionally substituted with one, two or three substituents independently selected from
  - (a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>R<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl,
  - (a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
  - (a-3) 5-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
  - (a-4) 6-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-

substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

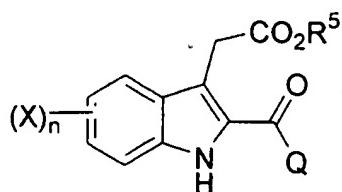
- (b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),
- (c) a 5-membered monocyclic aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);
- (d) C<sub>3-7</sub> cycloalkyl optionally substituted with one or two substituents independently selected from OH, C<sub>1-4</sub> alkyl, halo and halo-substituted C<sub>1-4</sub> alkyl; and
- (e) a benzo-fuzed heterocycle optionally substituted with one, two or three substituents independently selected from the group (a-1);

R<sup>2</sup> and R<sup>3</sup> are independently H, OH, C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkyl substituted with halo, OH, C<sub>1-4</sub> alkoxy, NH<sub>2</sub> or CN;

X is independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>NR<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl; and

n is 0, 1, 2, 3 or 4,

which process comprises reacting a compound of the formula:



7-VII

wherein R<sup>5</sup> is C<sub>1-6</sub> alkyl; Q, X and n are as defined as before, with a base in a suitable solvent.

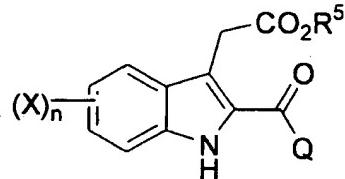
Preferred process of the above mentioned process is a process, wherein said base is sodium hydroxide, potassium hydroxide, sodium carbonate, potassium carbonate, 5 sodium bicarbonate, potassium bicarbonate, sodium t-pentoxide, sodium methoxide, sodium ethoxide or potassium t-butoxide.

Preferred process of the above mentioned process is a process, wherein said base is sodium hydroxide.

Preferred process of the above mentioned process is a process, wherein said 10 solvent is an aqueous mixture of methanol, ethanol, isopropyl alcohol or tetrahydrofuran.

Preferred process of the above mentioned process is a process, wherein said solvent is methanol containing water.

Also, the present invention provides a process for preparing a compound of the 15 formula:



7-VII

wherein

Q is selected from the following:

- 20 (a) phenyl optionally substituted with one, two or three substituents independently selected from  
 (a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>R<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl,

- (a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
- (a-3) 5-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
- (a-4) 6-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
- (b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),
- (c) a 5-membered monocyclic aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);
- (d) C<sub>3-7</sub> cycloalkyl optionally substituted with one or two substituents independently selected from OH, C<sub>1-4</sub> alkyl, halo and halo-substituted C<sub>1-4</sub> alkyl; and
- (e) a benzo-fused heterocycle optionally substituted with one, two or three substituents independently selected from the group (a-1);

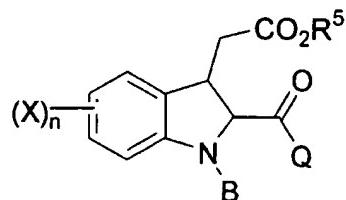
R<sup>2</sup> and R<sup>3</sup> are independently H, OH, C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkyl substituted

with halo, OH, C<sub>1-4</sub> alkoxy, NH<sub>2</sub> or CN;

X is independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, 5 aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>NR<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl; R<sup>5</sup> is C<sub>1-6</sub> alkyl; and

n is 0, 1, 2, 3 or 4,

which process comprises reacting a compound of the formula:



7-VI

10 wherein B, Q, X, n and R<sup>5</sup> are as defined above with a base in a suitable solvent.

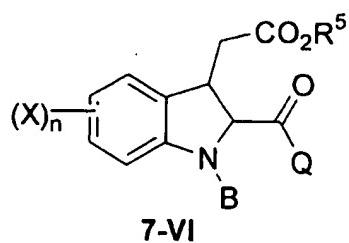
Preferred process of the above mentioned process is a process, wherein said base is 1,8-diazabicyclo[5.4.0]undec-7-ene, 1,5-diazabicyclo[4.3.0]non-5-ene, 1,1,3,3-tetramethylguanidine, sodium t-pentoxide, sodium methoxide, or potassium t-butoxide.

15 Preferred process of the above mentioned process is a process, wherein said base is 1,8-diazabicyclo[5.4.0]undec-7-ene or potassium t-butoxide.

Preferred process of the above mentioned process is a process, wherein said solvent is N,N-dimethylacetamide, N,N-dimethylformamide, methyl ethyl ketone, acetone, or tetrahydrofuran.

20 Preferred process of the above mentioned process is a process, wherein said solvent is N,N-dimethylacetamide.

Also, the present invention provides a process for preparing a compound of the formula:



wherein **B** is a suitable protecting group;

**Q** is selected from the following:

- (a) phenyl optionally substituted with one, two or three substituents independently selected from
  - (a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>R<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl,
  - (a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
  - (a-3) 5-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
  - (a-4) 6-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

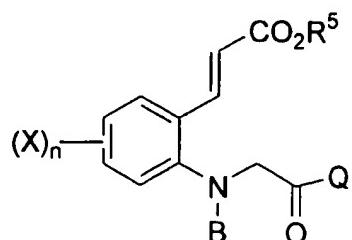
- (b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),
- 5 (c) a 5-membered monocyclic aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);
- 10 (d) C<sub>3-7</sub> cycloalkyl optionally substituted with one or two substituents independently selected from OH, C<sub>1-4</sub> alkyl, halo and halo-substituted C<sub>1-4</sub> alkyl; and
- (e) a benzo-fuzed heterocycle optionally substituted with one, two or three substituents independently selected from the group (a-1);

15 R<sup>2</sup> and R<sup>3</sup> are independently H, OH, C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkyl substituted with halo, OH, C<sub>1-4</sub> alkoxy, NH<sub>2</sub> or CN;

X is independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, 20 C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>NR<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl; R<sup>5</sup> is C<sub>1-6</sub> alkyl; and

n is 0, 1, 2, 3 or 4,

which process comprises reacting a compound of the formula:



wherein B, Q, X, n and R<sup>5</sup> are as defined above, with a base in the presence of a solvent.

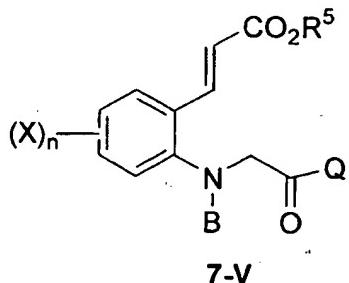
Preferred process of the above mentioned process is a process, wherein said base is potassium carbonate, potassium bicarbonate, sodium bicarbonate, sodium carbonate, or cesium carbonate.

Preferred process of the above mentioned process is a process, wherein said base is potassium carbonate.

Preferred process of the above mentioned process is a process, wherein said solvent is N,N-dimethylacetamide, N,N-dimethylformamide, methyl ethyl ketone, acetone, or tetrahydrofuran.

Preferred process of the above mentioned process is a process, wherein said solvent is N,N-dimethylacetamide.

Also, the present invention provides a process for preparing a compound of the formula:



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wherein B is a suitable protecting group;

Q is selected from the following:

- (a) phenyl optionally substituted with one, two or three substituents independently selected from
  - (a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>R<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl,

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- (a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
- 5 (a-3) 5-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
- 10 (a-4) 6-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
- 15 (b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),
- 20 (c) a 5-membered monocyclic aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);
- 25 (d) C<sub>3-7</sub> cycloalkyl optionally substituted with one or two substituents independently selected from OH, C<sub>1-4</sub> alkyl, halo and halo-substituted C<sub>1-4</sub> alkyl; and
- (e) a benzo-fuzed heterocycle optionally substituted with one, two or three substituents independently selected from the group (a-1);
- 30

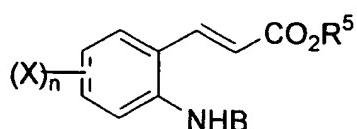
R<sup>2</sup> and R<sup>3</sup> are independently H, OH, C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkyl substituted

with halo, OH, C<sub>1-4</sub> alkoxy, NH<sub>2</sub> or CN;

X is independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>NR<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl; R<sup>5</sup> is C<sub>1-6</sub> alkyl; and

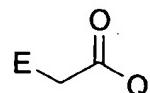
n is 0, 1, 2, 3 or 4,

which comprises reacting a compound of the formula:



7-II

wherein B, X, n and R<sup>5</sup> are as defined above, with a compound of the formula:



wherein E is halo and Q are as defined above, with a base in the presence of a solvent.

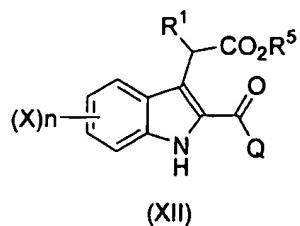
Preferred process of the above mentioned process is a process, wherein said base is potassium carbonate, potassium bicarbonate, sodium bicarbonate, sodium carbonate, or cesium carbonate.

Preferred process of the above mentioned process is a process, wherein said base is potassium carbonate.

Preferred process of the above mentioned process is a process, wherein said solvent is N,N-dimethylacetamide, N,N-dimethylformamide, methyl ethyl ketone, acetone or tetrahydrofuran.

Preferred process of the above mentioned process is a process, wherein said solvent is N,N-dimethylacetamide.

Also, the present invention provides a process for preparing a compound of the formula:



wherein

**Q** is selected from the following:

- (a) phenyl optionally substituted with one, two or three substituents independently selected from
  - (a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl,
  - (a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
  - (a-3) 5-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
  - (a-4) 6-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
- (b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being

optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4).

- (c) a 5-membered monocyclic aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);
  - (d) C<sub>3-7</sub> cycloalkyl optionally substituted with one or two substituents independently selected from OH, C<sub>1-4</sub> alkyl, halo and halo-substituted C<sub>1-4</sub> alkyl; and
  - (e) a benzo-fused heterocycle optionally substituted with one, two or three substituents independently selected from the group (a-1);

**R<sup>1</sup>** is hydrogen, C<sub>1-4</sub> alkyl or halo;

15 **R<sup>2</sup> and R<sup>3</sup>** are independently H, OH, C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkyl substituted with halo, OH, C<sub>1-4</sub> alkoxy, NH<sub>2</sub> or CN;

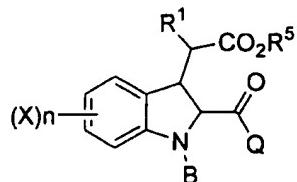
$R^5$  is C<sub>1-6</sub> alkyl;

**X** is independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino,

20  $C_{1-4}$  alkylamino, CN, HO-( $C_{1-4}$ ) alkyl,  $C_{1-4}$  alkoxy- $C_{1-4}$  alkyl,  $C_{1-4}$  alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>NR<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl,  $C_{1-4}$  alkylsulfonylamino and  $C_{3-7}$  cycloalkyl; and

**n** is 0, 1, 2, 3 or 4,

which process comprises treating a compound of the formula (X):

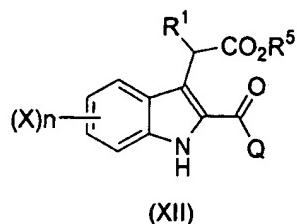


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(X)

wherein R<sup>1</sup>, R<sup>5</sup>, X, Q and n are as defined herein before, and B is a suitable protecting group, in the presence of a suitable base to obtain a compound of the formula (XII).

Also, the present invention provides a process for preparing a compound of the formula:



wherein

**Q** is selected from the following:

- (a) phenyl optionally substituted with one, two or three substituents independently selected from
  - (a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>R<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl,
  - (a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
  - (a-3) 5-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
  - (a-4) 6-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

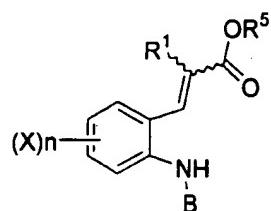
- (b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),
- 5 (c) a 5-membered monocyclic aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);
- 10 (d) C<sub>3-7</sub> cycloalkyl optionally substituted with one or two substituents independently selected from OH, C<sub>1-4</sub> alkyl, halo and halo-substituted C<sub>1-4</sub> alkyl; and
- (e) a benzo-fused heterocycle optionally substituted with one, two or three substituents independently selected from the group (a-1);
- 15

R<sup>1</sup> is hydrogen, C<sub>1-4</sub> alkyl or halo;

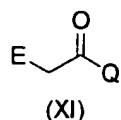
R<sup>2</sup> and R<sup>3</sup> are independently H, OH, C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkyl substituted with halo, OH, C<sub>1-4</sub> alkoxy, NH<sub>2</sub> or CN;

R<sup>5</sup> is C<sub>1-6</sub> alkyl;

- 20 X is independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>NR<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl; and
- 25 n is 0, 1, 2, 3 or 4,
- which process comprises reacting a compound of the formula (IX):



wherein  $R^1$ ,  $R^5$ ,  $X$ , and  $n$  are as defined above, and  $B$  is a suitable protecting group, with a compound of the formula (XI):



wherein  $E$  is halo and  $Q$  is as defined as before, in the presence of a suitable base at a temperature of  $-40$  °C to  $200$  °C to obtain a compound of the formula (XII).

Preferred process of the above mentioned process is a process, wherein the reaction is carried out at a temperature of  $0$  °C to  $100$  °C

Preferred process of the above mentioned process is a process, wherein the suitable base is potassium carbonate, cesium carbonate, sodium carbonate, sodium tert-butoxide, potassium tert-butoxide, sodium hydride, potassium hydride or potassium fluoride.

Preferred process of the above mentioned process is a process, wherein the reaction is firstly carried out in the presence of a base for 2 minutes to a day; and then, another base is added to the reaction mixture.

Preferred process of the above mentioned process is a process, wherein the reaction is firstly carried out for 30 minutes to 8 hours.

Preferred process of the above mentioned process is a process, wherein the suitable protecting group is methoxycarbonyl, ethoxycarbonyl, tert-butoxycarbonyl, benzyloxycarbonyl, phenylsulfonyl, p-toluenesulfonyl, methanesulfonyl or trifluoromethanesulfonyl.

Preferred process of the above mentioned process is a process, wherein the suitable protecting group is phenylsulfonyl, p-toluenesulfonyl, methanesulfonyl or trifluoromethanesulfonyl.

Preferred process of the above mentioned process is a process, wherein the first base is selected from sodium *tert*-butoxide, potassium *tert*-butoxide, sodium carbonate, potassium carbonate, cesium carbonate, sodium hydride, potassium hydride, sodium carbonate, potassium carbonate, cesium carbonate, potassium fluoride, 1,8-diazabicyclo[5.4.0]undec-7-ene, 1,5-diazabicyclo[4.3.0]non-5-ene, 1,4-diazabicyclo[2.2.2]octane, pyridine, pyrrolidine, triethylamine, diisopropylamine, diisopropylethylamine and diethylisopropylamine; and the second base is selected from sodium *tert*-butoxide, potassium *tert*-butoxide, sodium carbonate, potassium carbonate, cesium carbonate, sodium hydride, potassium hydride, sodium carbonate, potassium carbonate, cesium carbonate, potassium fluoride, 1,8-diazabicyclo[5.4.0]undec-7-ene, 1,5-diazabicyclo[4.3.0]non-5-ene, 1,4-diazabicyclo[2.2.2]octane, pyridine, pyrrolidine, triethylamine, diisopropylamine, diisopropylethylamine and diethylisopropylamine.

Preferred process of the above mentioned process is a process, wherein the first base is selected from potassium carbonate, cesium carbonate, sodium hydride and potassium fluoride; and the second base is selected from 1,8-diazabicyclo[5.4.0]undec-7-ene, cesium carbonate, pyrrolidine, diisopropylamine, triethylamine, diethylisopropylamine and diisopropylethylamine.

Preferred process of the above mentioned process is a process, wherein the first base is potassium carbonate, cesium carbonate or potassium fluoride; and the second base is 1,8-diazabicyclo[5.4.0]undec-7-ene, potassium *tert*-butoxide or cesium carbonate.

Preferred process of the above mentioned process is a process, wherein the combination of the first base and the second base (first base/second base) is selected from potassium carbonate/1,8-diazabicyclo[5.4.0]undec-7-ene, potassium carbonate/cesium carbonate, cesium carbonate/potassium *tert*-butoxide, cesium carbonate/1,8-diazabicyclo[5.4.0]undec-7-ene and potassium fluoride/1,8-diazabicyclo[5.4.0]undec-7-ene and potassium fluoride/cesium carbonate.

Preferred process of the above mentioned process is a process, wherein the combination of the first base and the second base (first base/second base) is selected

substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

- (b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),
- (c) a 5-membered monocyclic aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);
- (d) C<sub>3-7</sub> cycloalkyl optionally substituted with one or two substituents independently selected from OH, C<sub>1-4</sub> alkyl, halo and halo-substituted C<sub>1-4</sub> alkyl; and
- (e) a benzo-fuzed heterocycle optionally substituted with one, two or three substituents independently selected from the group (a-1);

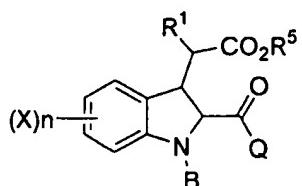
R<sup>1</sup> is hydrogen, C<sub>1-4</sub> alkyl or halo;

R<sup>2</sup> and R<sup>3</sup> are independently H, OH, C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkyl substituted with halo, OH, C<sub>1-4</sub> alkoxy, NH<sub>2</sub> or CN;

X is independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>NR<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl; and

n is 0, 1, 2, 3 or 4,

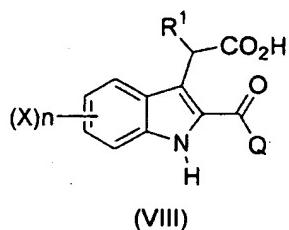
which process comprises treating a compound of the formula (X):



(X)

wherein R<sup>1</sup>, R<sup>5</sup>, X, Q and n are as defined here before, with a suitable base under hydrolyzing conditions to obtain the compound of formula (VIII).

This invention also provides a process for preparing a compound of the formula  
5 (VIII):



wherein

**Q** is selected from the following:

- (a) phenyl optionally substituted with one, two or three substituents independently selected from
  - (a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>R<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl,
  - (a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
  - (a-3) 5-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub>

<sub>4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

(a-4) 6-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

- (b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),
- (c) a 5-membered monocyclic aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);
- (d) C<sub>3-7</sub> cycloalkyl optionally substituted with one or two substituents independently selected from OH, C<sub>1-4</sub> alkyl, halo and halo-substituted C<sub>1-4</sub> alkyl; and
- (e) a benzo-fused heterocycle optionally substituted with one, two or three substituents independently selected from the group (a-1);

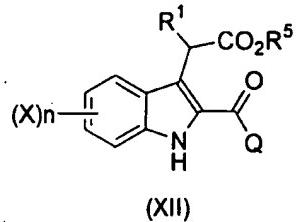
R<sup>1</sup> is hydrogen, C<sub>1-4</sub> alkyl or halo;

R<sup>2</sup> and R<sup>3</sup> are independently H, OH, C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkyl substituted with halo, OH, C<sub>1-4</sub> alkoxy, NH<sub>2</sub> or CN;

X is independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>NR<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl; and

n is 0, 1, 2, 3 or 4,

which process comprises hydrolyzing a compound of the formula (XII):

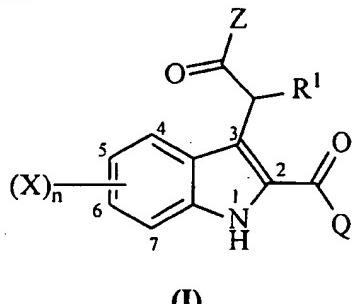


wherein  $R^5$  is  $C_{1-6}$  alkyl,  $R^1$ , X, Q and n are as defined herein before.

5

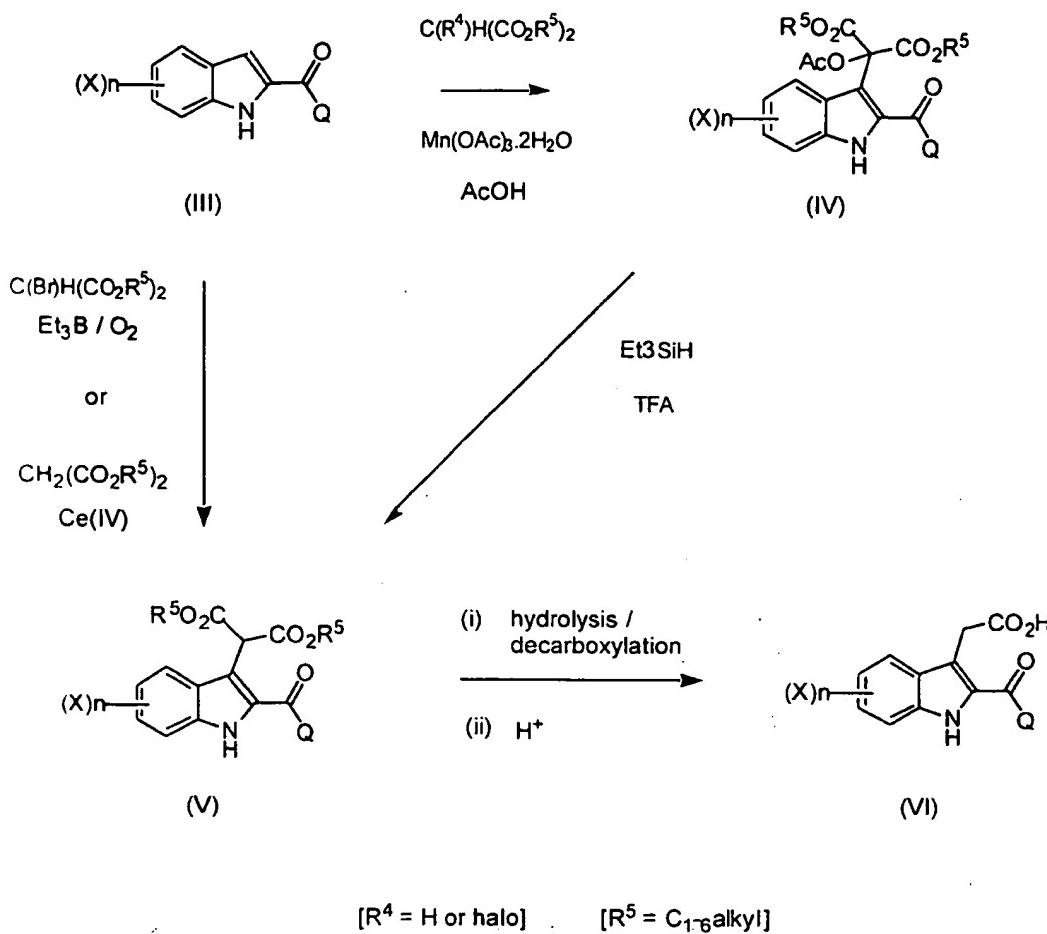
#### General Synthesis

A compound of general formula (I) may be prepared by any synthetic procedure applicable to structure-related compounds known to those skilled in the art. The following representative examples as described hereinafter are illustrative and are not meant to limit the scope of the invention in anyway. Unless otherwise stated, Q, X, Z, 10  $R^1$ , and n are as defined above.



#### Scheme 1:

In one embodiment, for example, a compound of the formula (VI) may be 15 prepared according to the reaction sequences depicted in Scheme 1. (Compound (VI) corresponds to a compound (I) wherein  $R^1$  is H, and Z is OH.)

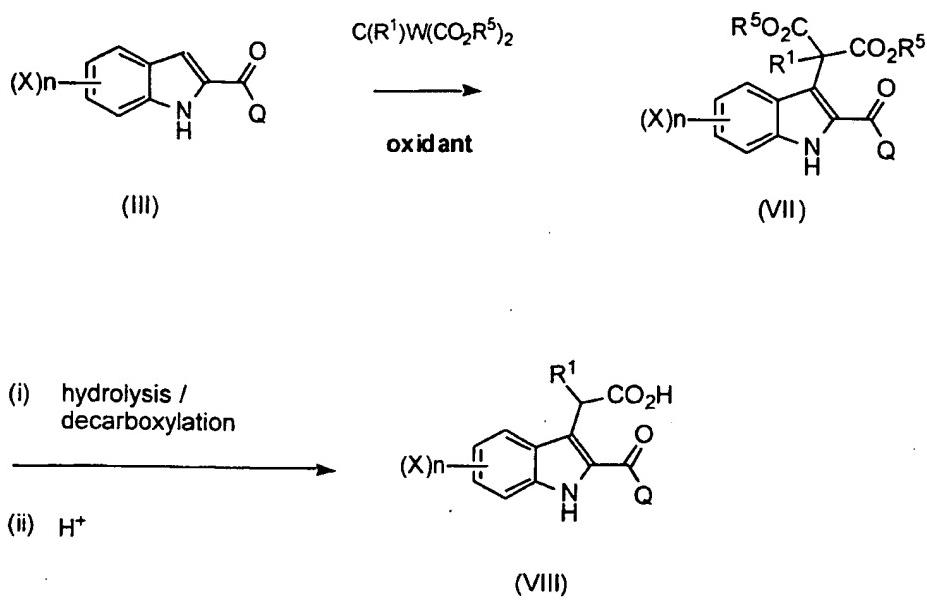
**Scheme 1**

In brief, a compound of formula (III) is subjected to oxidative homolytic malonylation (for leading references see J. M. Muchowski et al; Can. J. Chem., 70, 1838, 1992 and E. Baciocchi et al; J. Org. Chem., 58, 7610, 1993). In one example, a compound of the formula (III) is reacted with a suitable malonyl radical generated from a compound of formula  $\text{C}(\text{R}^4)\text{H}(\text{CO}_2\text{R}^5)_2$ , wherein  $\text{R}^4$  is hydrogen or halogen, preferably chloro, and  $\text{R}^5$  is  $\text{C}_{1-6}$  alkyl, and a manganese(III) agent, preferably manganese (III) triacetate. The manganese(III) agent is usually used in stoichiometric amounts but, alternatively, may be made catalytic by use of a suitable reoxidizing agent such as sodium persulfate, usually in the presence of a co-catalyst such as, a silver(I) salt such as silver nitrate. A preferred reaction solvent is acetic acid; however, acetic acid-acetic anhydride or other protic solvents such as propionic acid can be used. The reaction is preferably conducted in the presence of sodium acetate or potassium acetate, but, may be conducted in solvent alone. Reaction temperatures are generally in the range of room temperature (e.g., 25 °C) to reflux temperature of solvent, preferably 60

to 100 °C, but if necessary, lower or higher temperature can be employed. Reaction times are, in general, from one hour to a day, preferably from 4 to 16 hours, however shorter or longer reaction times, if necessary, can be employed. In the immediate instance, the  $\alpha$ -acetoxy compounds of formula (IV) is usually obtained as the major product. Compounds of formula (IV) can readily be transformed to compounds of formula (V) by reduction with a suitable reducing agent, for example, a trialkylsilane, sodium  $\alpha$ -(dimethylamino)napthalenide, lithium in liquid ammonia, sodium napthalenide, preferably triethylsilane in a suitable protic solvent, notably, trifluoroacetic acid. Alternatively, the reaction can be conducted in a reaction inert co-solvent such as dichloromethane or 1,2-dichloroethane. Reaction temperatures are generally in the range of room temperature to reflux temperature of solvent, preferably 15 to 100 °C, but if necessary, lower or higher temperature can be employed. Reaction times are, in general, from several minutes to a day, preferably from 20 minutes to 5 hours, however shorter or longer reaction times, if necessary, can be employed. Alternatively, a compound of formula (V) may be obtained directly from a compound of formula (III) from a malonyl radical generated from (i) a suitable monohalomalonate, preferably, bromomalonate, mediated by aerial oxidation of a trialkylborane such as triethylborane (see B. Giese; In Radicals in organic synthesis formation of carbon-carbon bonds. Pergamon Press, Oxford. pp. 86-89, 1986, and P. G. Allies and P. B. Brindley; J. Chem. Soc. (B), 1126, 1960) or, (ii) a malonic ester in the presence of a cerium(IV) salt such as cerium (IV) ammonium nitrate (for example, see E. Baciocchi et al; Tetrahedron Lett, 2763, 1986). A compound of formula (V) may be readily transformed to a compound of formula (VI) by subjection to standard saponification / decarboxylation conditions.

25 **Scheme 2:**

Alternatively, as depicted in Scheme 2, a compound of the formula (VIII) (a compound (I) wherein Z is OH), wherein R<sup>1</sup> is C<sub>1-4</sub> alkyl, may be prepared in an analogous manner to that of a compound of formula (VI) employing appropriate reaction conditions as described by illustration herein above from a suitable monoalkylmalonate, wherein R<sup>1</sup> is C<sub>1-4</sub> alkyl, W is hydrogen or a halogen, preferably bromide, and R<sup>5</sup> is C<sub>1-6</sub> alkyl, from a compound of formula (III).



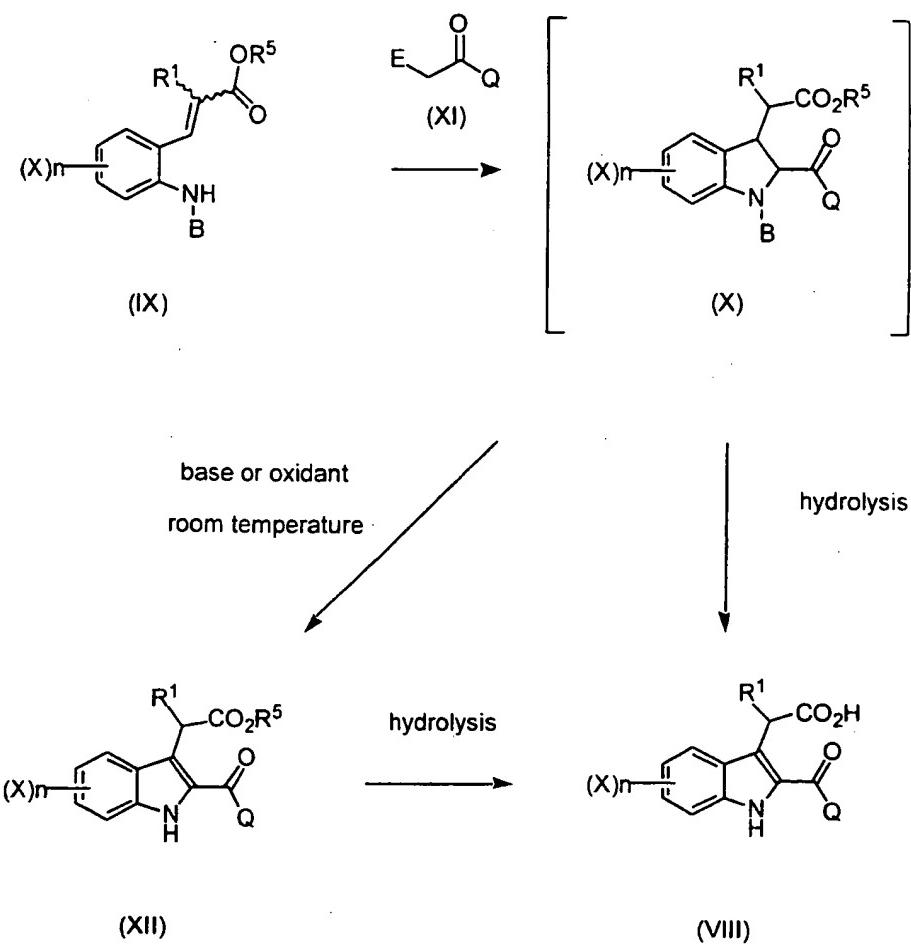
[ $R^1$  is not hydrogen]      [ $W = H$  or halo]      [ $R^5 = C_{1-6}$  alkyl]

### Scheme 2

In Scheme 2, for example, the oxidant is manganese (III) agent such as manganese (III) triacetate, or Cerium (IV) agent such as ammonium Cerium (IV) nitrate and Cerium (IV) sulfate.

### Scheme 3:

In another embodiment, a compound of formula (VIII) is readily accessible from the appropriate 2-aminocinnamic acid ester (IX) wherein B is a suitable protecting group, for example, methoxycarbonyl, ethoxycarbonyl, tert-butoxycarbonyl (Boc), benzyloxycarbonyl, phenylsulfonyl, p-toluenesulfonyl, methanesulfonyl, trifluoromethanesulfonyl, methanesulfonyl or trifluoromethanesulfonyl (preferably phenylsulfonyl, p-toluenesulfonyl, methanesulfonyl or trifluoromethanesulfonyl).



[R<sup>5</sup> = C<sub>1-6</sub>alkyl]

[B = a suitable protecting group]

[E = halogen]

### Scheme 3

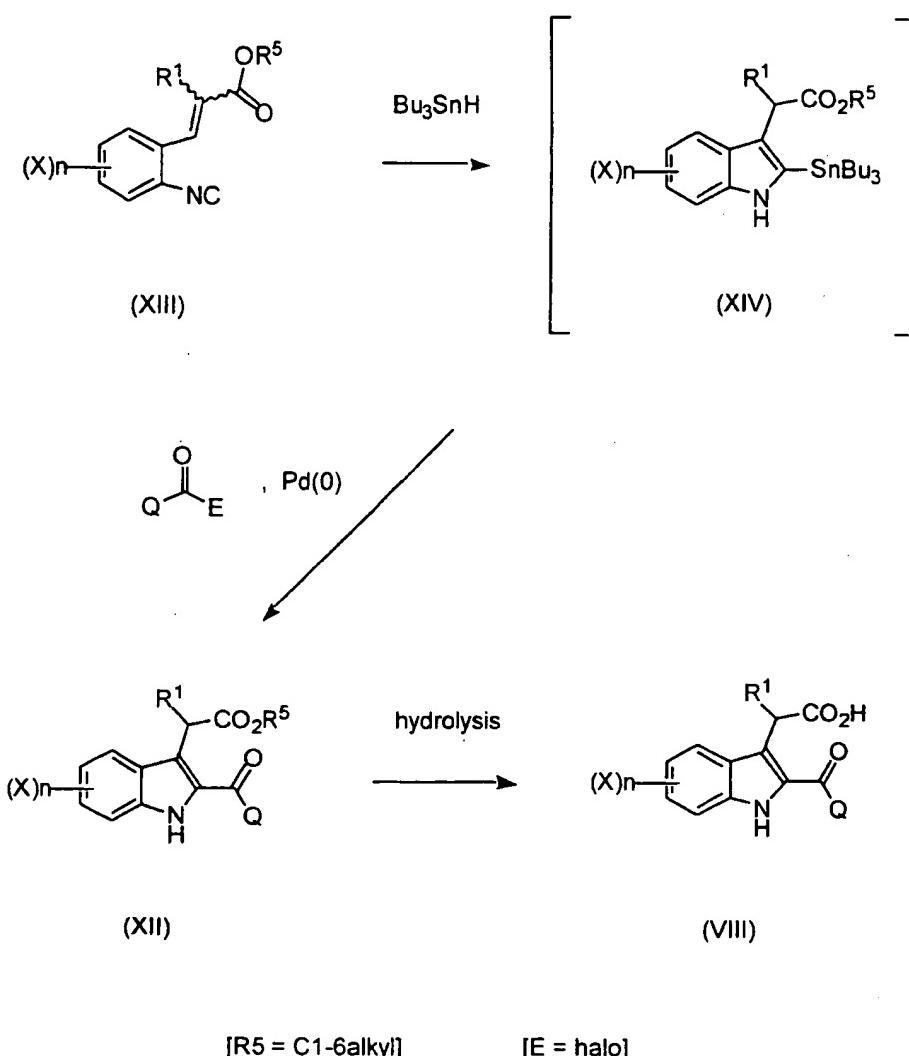
In Scheme 3, the requisite 2-aminocinnamic acid ester (IX) is reacted with a compound of formula (XI), wherein Q is as defined above and E is halogen, preferably, iodo, bromo or chloro, in the presence of a suitable base. A suitable base is, for example, an alkali or alkaline earth metal alkoxide, carbonate, fluoride or hydride, such as sodium *tert*-butoxide, potassium *tert*-butoxide, sodium carbonate, potassium carbonate, cesium carbonate, sodium hydride, potassium fluoride or potassium hydride. Preferred reaction inert solvents include, but are not limited to, acetone, methyl ethyl ketone, acetonitrile, N,N-dimethylformamide (DMF), N,N-dimethylacetamide (DMA), dimethylsulfoxide (DMSO), dioxane or tetrahydrofuran (THF). Reaction temperatures are preferably in the range of -40 °C to reflux temperature of solvent (for example 200 °C), usually in the range of 0 °C to 100 °C, but if necessary, lower or higher temperature can be employed. Reaction time is in general from 2 minutes to a

day, preferably from 30 minutes to 8 hours, however shorter or longer reaction times, if necessary, can be employed. When the reaction is, for example, conducted at room temperature (e.g., 25 °C) the intermediate indoline (X) can be isolated. Reaction at higher temperatures (e.g., 40 to 100 °C) can result in formation of indole (XII).

5     Usually the intermediate indoline (X) is not isolated but either (i) hydrolyzed with commitant formation of the indole ring directly to a compound of formula (VIII) under standard conditions known to those skilled in the art, or (ii) transformed to a compound of formula (XII) by using a suitable base, for example, an alkali or alkaline earth metal carbonate such as sodium carbonate, potassium carbonate or cesium carbonate, or an  
10    organic base such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), 1,4-diazabicyclo[2.2.2]octane (DABCO), pyridine, pyrrolidine, triethylamine, diisopropylamine, diisopropylethylamine, diethylisopropylamine, Hunig's base, potassium tert-butoxide, sodium tert-butoxide, or the like, or a suitable oxidant such as cerium (IV) ammonium nitrate (CAN),  
15    manganese(IV) oxide, manganese(III) triacetate, copper (II) acetate / air, chloranil, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), N-methylmorpholine-N-oxide, or the like (for example, see H. Dumoulin et al; J. Heterocycl. Chem., 32, 1703, 1995; H. Rapoport et al; Tetrahedron Lett., 5053, 1991; P. Martin et al; Helv. Chim. Acta, 77, 111, 1994; Y. Kikugawa et al, J. Chem. Soc. Perkins Trans 1, 7, 1401, 1984; A.  
20    Goti et al; Tetrahedron Lett., 6567, 1996; L. S. Liebeskind et al; J. Org. Chem, 61, 2594, 1996). Preferred reaction inert solvents include, but are not limited to, acetone, methyl ethyl ketone, acetonitrile, dioxane or tetrahydrofuran (THF). Reaction temperatures are preferably in the range of 0 °C to reflux temperature of solvent, usually in the range of 15 to 60 °C, but if necessary, lower or higher temperature can be  
25    employed. Reaction time is in general from several minutes to a day, preferably from 30 minutes to 8 hours, however shorter or longer reaction times, if necessary, can be employed. A compound of formula (XII) may be readily hydrolyzed to a compound of formula (VIII) under standard conditions.

**Scheme 4:**

30     In another embodiment, a compound of formula (VIII), wherein Q, X, R<sup>1</sup> and n are as defined above, may be prepared as illustrated in Scheme 4.

**Scheme 4**

For example, treatment of a compound of formula (XIII), wherein R<sup>1</sup>, R<sup>2</sup>, X and n are as defined above, with a trialkyltin hydride, e.g., tributyltin hydride usually in the presence of a radical initiator such as, 2,2'-azobisisobutyronitrile (AIBN), affords the intermediate 2-stannylinde (XIV) via an intramolecular radical cyclization as described in J. Am. Chem. Soc., 116, 3127, (1994); T. Fukuyama et al. The intermediate (XIV) generated *in situ* is subsequently treated with an acyl halide, wherein Q and E are as defined above, in the presence of a suitable palladium catalyst according to Stille's procedure (for example see. J. K. Stille et al; J. Am. Chem. Soc., 109, 813, 5478, (1987) and J. Am. Chem. Soc., 106, 4833, (1984)) to afford indole (XII) which may be hydrolyzed to a compound of formula (VIII) by conventional

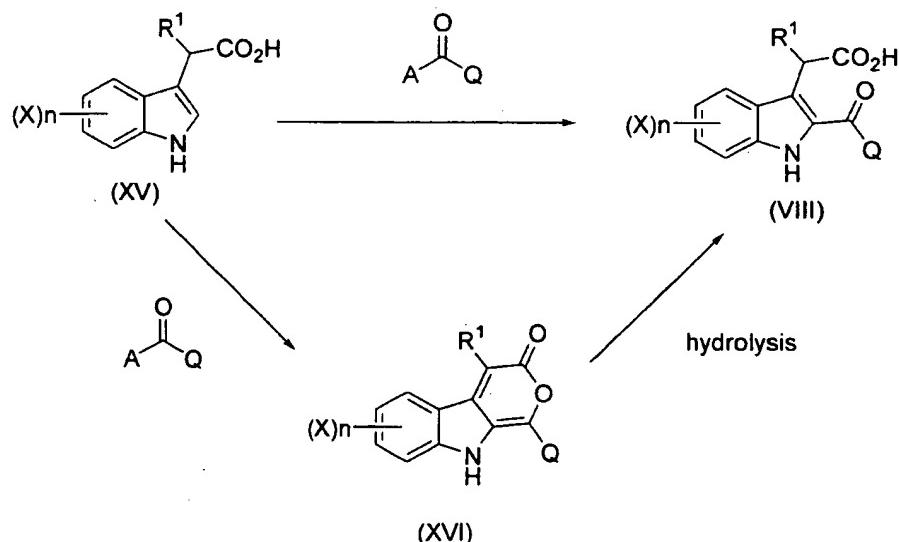
procedure.

Examples of the palladium catalyst are tetrakis(triphenylphosphine)palladium(0), dichlorobis(triphenylphosphine)palladium(II), bis(dibenzylideneacetone)palladium(0), 5 benzyl(chloro)bis(triphenylphosphine)palladium(II), bis(acetonitrile)dichloropalladium(II).

**Scheme 5:**

In another embodiment, a compound of formula (VIII), wherein Q, X, R<sup>1</sup> and n are as defined above, may be prepared as illustrated in Scheme 5.

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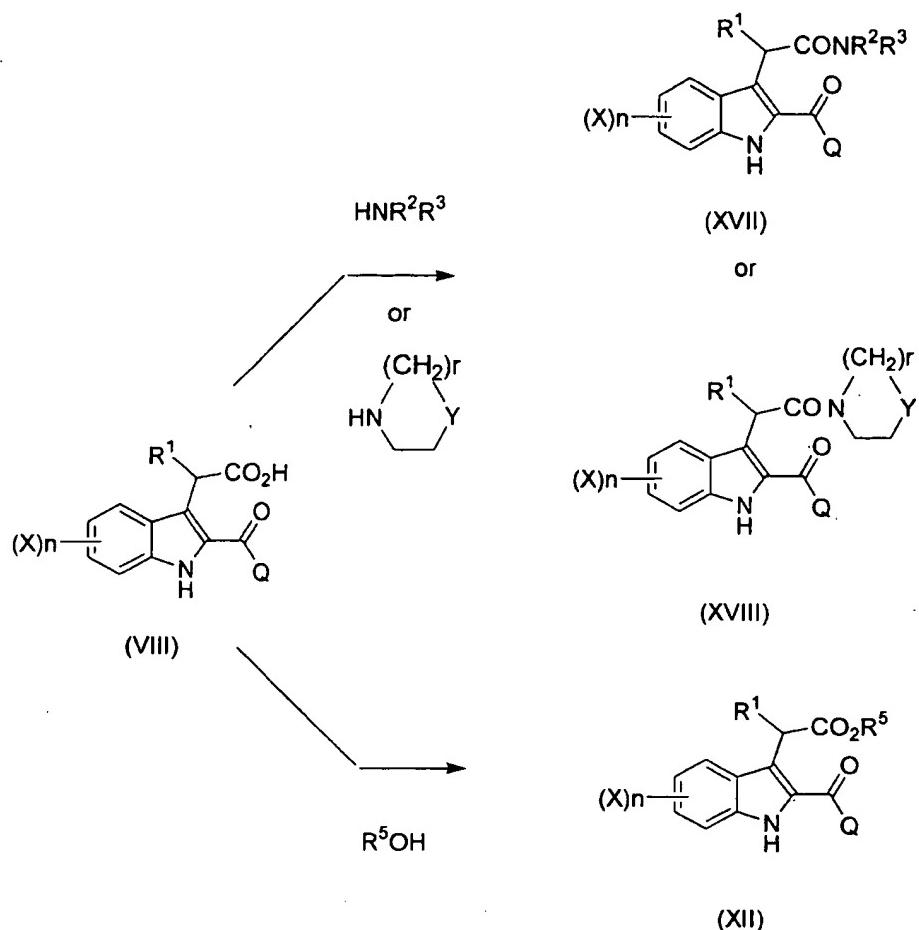
**Scheme 5**

For example, treatment of a compound (XV), wherein R<sup>1</sup>, X and n are as defined above, is reacted with a compound of formula Q-C(O)-A affords a compound 15 of formula (VIII), or a compound of formula (XVI) (for example see U.Pindur et al., *Liebigs Ann. Chem.*, 601 (1991) and C.J.Moody et al., *J.Chem.Soc.Perkin Trans.I*, 3249 (1988)) which may be hydrolyzed to a compound of formula (VIII) by conventional procedure (for example see E.B.Fray et al., *Tetrahedron*, 49, 439 (1993) and U.Pindur et al., *J.Heterocycl.Chem.*, 29, 145 (1992)). In a compound of formula 20 A-C(O)-Q, A is defined such that the compound of A-C(O)-Q is, for example, an acyl halide, carboxylic acid, carboxylic acid anhydride, a mixed carboxylic sulfonic

anhydride, or the like. The reaction may be conducted in the presence or absence of catalyst, preferably in the presence of catalyst such as, boron trifluoride-diethyl ether, tin(IV) chloride, aluminum chloride, ferric chloride, zinc chloride, iodine, iron, or the like. Preferred reaction inert solvents include, but are not limited to, diethyl ether, 5 dichloromethane, 1,2-dichloroethane, carbon disulfide, nitrobenzene or nitromethane. Reaction temperatures are preferably in the range of -78 to 210 °C, usually in the range of -10 °C to reflux temperature of solvent, but if necessary, lower or higher temperature can be employed. Reaction time is in general from several minutes to a day, preferably from 30 minutes to 8 hours, however shorter or longer reaction times, if 10 necessary, can be employed.

**Scheme 6:**

Acetic acid compounds of formulae (VI) and (VIII) as described in the aforementioned schemes may be readily transformed to the corresponding amide, 15 compounds of formulae (XVII) and (XVIII), or ester, compound of formula (XII), by any conventional method known to those skilled in the art.



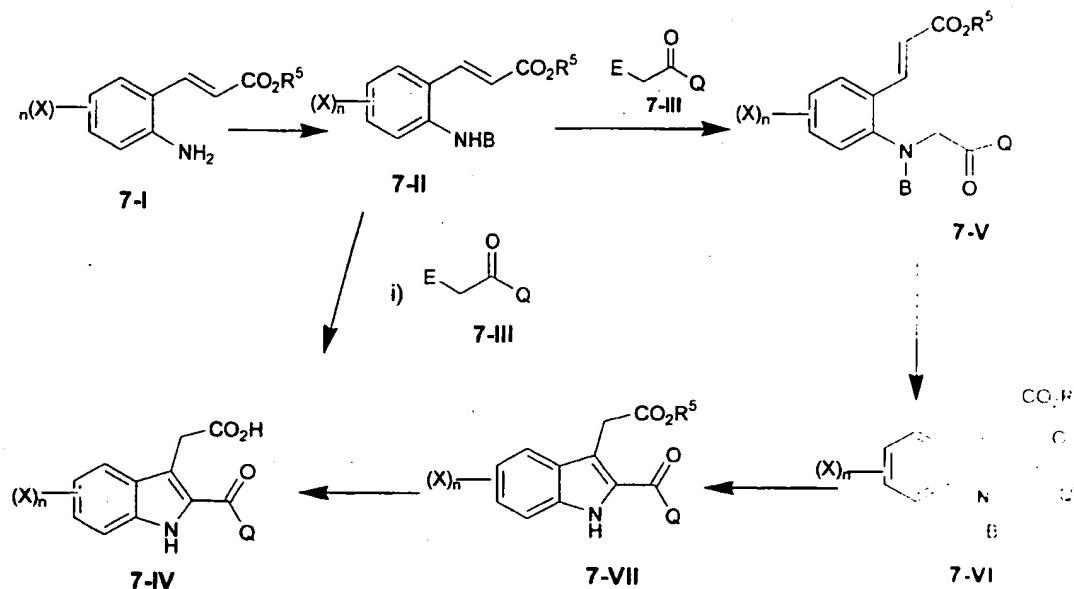
[ $\text{R}^5 = \text{C}_{1-6}\text{alkyl}$ ]

**Scheme 6**

As depicted in Scheme 6, compounds of formulae (XVII) and (XVIII) can be readily prepared by treating the requisite acetic acid compounds of formulae (VI) and 5 (VIII) with an appropriate amine, wherein  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{Y}$  and  $r$  are as described herein before, in the presence of a suitable coupling reagent such as, but not limited to, 1-(dimethylaminopropyl)-3-ethylcarbodiimide (WSC),  $\text{N},\text{N}'$ -dicyclohexylcarbodiimidazole (DCC), carbonyldiimidazole, diethylphosphorocyanidate (DEPC), or the like. Preferred reaction inert solvents include, but are not limited to, 10 acetone, acetonitrile, dichloromethane, 1,2-dichloroethane,  $\text{N},\text{N}$ -dimethylformamide (DMF),  $\text{N},\text{N}$ -dimethylacetamide (DMA), dimethylsulfoxide (DMSO), dioxane, tetrahydrofuran (THF) or pyridine. Reaction temperatures are preferably in the range of -40 to 150 °C, usually in the range of 15 °C to reflux temperature of solvent, but if

necessary, lower or higher temperature can be employed. Reaction time is in general from several minutes to a day, preferably from 30 minutes to 8 hours, however shorter or longer reaction times, if necessary, can be employed. The compounds of formulae (VI) and (VIII) can also be readily transformed to the corresponding ester by conventional methods.

**Scheme 7**



(wherein B is a suitable protecting group, R<sup>5</sup> is C<sub>1-6</sub> alkyl, E is halo, Q, X and n is as defined above.)

In Scheme 7, the starting material of formula 7-I may be prepared according to methods familiar to those of ordinary skill in the art, including one or more synthetic procedures described in R. W. Carling, P. D. Leeson, K. Moore, J. D. Smith, C. R. Moyes, *J. Med. Chem.*, 1993, pages 3397-3408.

The compound of formula 7-II is prepared from a compound of formula 7-I by treatment with a base and an electrophile in a suitable solvent. Suitable bases include such as triethylamine, diisopropylethylamine, or pyridine optionally substituted by 1 to 3 (C<sub>1</sub>-C<sub>4</sub>)alkyl groups, preferably pyridine. Suitable electrophiles include methanesulfonyl chloride or anhydride, or phenylsulfonyl chloride wherein the phenyl moiety of said phenylsulfonyl optionally includes 1 or 2 substituents selected from halo, nitro, and (C<sub>1</sub>-C<sub>4</sub>)alkyl. Suitable solvents include dichloromethane, dichloroethane,

methyl *t*-butyl ether, disopropyl ether or toluene, preferably dichloromethane. The temperature of the aforesaid reaction may range from about 0 °C to about 50 °C, preferably about room temperature (20-25 °C) for a period of about 1 to 30 hours, preferably about 18 hours.

5       The compound of formula 7-IV is prepared from a compound of formula 7-II by treatment with a first base and an alkylating agent of the formula 7-III in the presence of a solvent followed by reaction with a second base followed by reaction with an acid.. Suitable first bases include potassium carbonate, potassium bicarbonate, sodium bicarbonate, sodium carbonate or cesium carbonate, preferably 10 potassium carbonate. Suitable solvents include *N,N*-dimethylacetamide, *N,N*-dimethylformamide, methyl ethyl ketone, acetone or tetrahydrofuran, preferably *N,N*-dimethylacetamide. The aforesaid reaction is performed at a temperature ranging from about 0 °C to about 100 °C, preferably room temperature (20-25 °C), for a period of time of about 10 minutes to 5 hours, typically 15 minutes. Suitable second 15 bases include an aqueous solution of a base such as sodium hydroxide, potassium hydroxide, sodium carbonate, potassium carbonate, sodium *t*-pentoxide (followed by water), sodium methoxide (followed by water) or potassium *t*-butoxide (followed by water), preferably sodium hydroxide. The reaction with the second base is performed at a temperature ranging from about 20 °C to about 120 °C, preferably 100 °C, for a 20 period of time of about 1 hour to 24 hours, typically 8 hours. Suitable acids include aqueous hydrochloric acid, hydrobromic acid, sulfuric acid or ammonium chloride, preferably hydrochloric acid. The reaction with the acid is performed at a temperature ranging from about 0 °C to about 50 °C, preferably about 20 °C to about 25 °C, for a period of time of about 1/2 hour to about 6 hours, typically about 1 hour.

25       Alternatively, the conversion of the compound of formula 7-II to a compound of formula 7-IV can be accomplished stepwise. The compound of formula 7-V may be prepared from a compound of formula 7-II by treatment with a base and an alkylating agent of formula 7-III in the presence of a solvent. Suitable bases include potassium carbonate, potassium bicarbonate, sodium bicarbonate, sodium carbonate, or 30 cesium carbonate, preferably potassium carbonate. Suitable solvents include *N,N*-dimethylacetamide, *N,N*-dimethylformamide, methyl ethyl ketone, acetone or

tetrahydrofuran, preferably *N,N*-dimethylacetamide. The temperature for the aforesaid reaction may range from about 0 °C to about 50 °C, preferably room temperature (20-25 °C), for a period of time of about 10 minutes to 40 minutes, typically 30 minutes.

- 5       The compound of formula 7-VI is prepared from a compound of formula 7-V by reaction with a base in the presence of a solvent. Suitable bases include potassium carbonate, potassium bicarbonate, sodium bicarbonate, sodium carbonate or cesium carbonate, preferably potassium carbonate. Suitable solvents include *N,N*-dimethylacetamide, *N,N*-dimethylformamide, methyl ethyl ketone, acetone or tetrahydrofuran, preferably *N,N*-dimethylacetamide. The temperature for the aforesaid reaction may range from about 0 °C to about 50 °C, preferably room temperature (20-25 °C), for a period of time of about 1 hour to 6 hours, preferably 4 hours.

- 10      The compound of formula 7-VII is prepared from a compound of formula 7-VI by reaction with a base in a suitable solvent. Suitable bases include 1,8-diazabicyclo[5.4.0]undec-7-ene, 1,5-diazabicyclo[4.3.0]non-5-ene, 1,1,3,3-tetramethylguanidine, sodium t-pentoxide, sodium methoxide or potassium *t*-butoxide, preferably 1,8-diazabicyclo[5.4.0]undec-7-ene methoxide or potassium *t*-butoxide. Suitable solvents include *N,N*-dimethylacetamide, *N,N*-dimethylformamide, methyl ethyl ketone, acetone or tetrahydrofuran, preferably *N,N*-dimethylacetamide. The temperature for the aforesaid reaction may range from about 0 °C to 100 °C, preferably room temperature (20-25 °C), for a period of 30 minutes to 5 hours, preferably 1 hour.

- 15      The compound of formula 7-IV is prepared from a compound of formula 7-VII by treatment with a base in a suitable solvent. Suitable bases include sodium hydroxide, potassium hydroxide, sodium carbonate, potassium carbonate, sodium bicarbonate, potassium bicarbonate, sodium t-pentoxide, sodium methoxide, sodium ethoxide or potassium *t*-butoxide, preferably sodium hydroxide. Suitable solvents include an aqueous mixture of methanol, ethanol, isopropyl alcohol or tetrahydrofuran, preferably methanol, containing water. The temperature of the aforesaid reaction may range from about 10 °C to 100 °C, preferably room temperature (20-25 °C), for a

period of 12 to 48 hours, preferably 24 hours, to provide the carboxylate salt of compound of formula 7-IV which can then be treated with an acid to provide the compound of formula 7-IV.

The compound of formula 7-VI has asymmetric atoms and therefore exist in  
5 different enantiomeric and diastereomeric forms. Diastereomeric mixtures can be separated into their individual diastereomers on the basis of their physical chemical differences by methods known to those skilled in the art, for example, by chromatography or fractional crystallization. The use of all such isomers, including diastereoisomer mixtures and pure enantiomers, are considered to be part of the present  
10 invention.

The starting materials in the aforementioned general syntheses may be obtained by conventional methods known to those skilled in the art. The preparation of such starting materials is described within the accompanying non-limiting examples which are provided for the purpose of illustration only. Alternatively, requisite starting  
15 materials may be obtained by analogous procedures, or modifications thereof, to those described hereinafter.

The products which are addressed in the aforementioned general syntheses and illustrated in the experimental examples described herein after may be isolated by standard methods and purification can be achieved by conventional means known to  
20 those skilled in the art, such as distillation, crystallization or chromatography techniques.

Certain compounds described herein contain one or more asymmetric centers and are capable of existing in various stereoisomeric forms. The present invention contemplates all such possible stereoisomers as well as their racemic and resolved,  
25 enantiomerically pure forms and pharmaceutically acceptable salts thereof.

Certain compounds of the present invention are capable of forming addition salts with inorganic or organic acids. The pharmaceutically acceptable acid salts of the compounds of formula (I) are those which form non-toxic addition salts, such as, but not limited to, the hydrochloride, hydrobromide, sulfate or bisulfate, acetate,  
30 benzoate, besylate, citrate, fumarate, glucuronate, hippurate, lactate, tartrate, saccharate, succinate, maleate, methanesulfonate, *p*-toluenesulfonate, phosphate and pamoate (i.e.,

4,4'-methylene-bis-(3-hydroxy-2-naphthoate)) salts. The pharmaceutically acceptable acid salts may be prepared by conventional techniques.

- Certain compounds of the present invention are capable of forming pharmaceutically acceptable non-toxic cations. Pharmaceutically acceptable non-
- 5 toxic cations of compounds of formula (I) may be prepared by conventional techniques by, for example, contacting said compound with a stoichiometric amount of an appropriate alkali or alkaline earth metal (sodium, potassium, calcium and magnesium) hydroxide or alkoxide in water or an appropriate organic solvent such as ethanol, isopropanol, mixtures thereof, or the like.
- 10 Also included within the scope of this invention are bioprecursors (also called pro-drugs) of the compounds of the formula (I). A bioprecursor of a compound of the formula (I) is a chemical derivative thereof which is readily converted back into the parent compound of the formula (I) in biological systems. In particular, a bioprecursor of a compound of the formula (I) is converted back to the parent compound of the formula (I) after the bioprecursor has been administered to, and absorbed by, a mammalian subject, e.g., a human subject. When the compounds of the formula (I) of this invention may form solvates such as hydrates, such solvates are included within the scope of this invention.
- 15

An example of prodrug of the compound of formula (I) is a compound of the formula (I), wherein the 1st position of indole ring is substituted with a group selected from hydroxymethyl, -C(O)-C<sub>1-4</sub> alkyl, -C(O)-(NH<sub>2</sub>)CH-(C<sub>1-4</sub> alkyl), -C(O)-phenyl, CH<sub>2</sub>NHC(O)-aryl, -CH<sub>2</sub>-C<sub>1-4</sub>alkyl-O-C(O)-C<sub>1-4</sub>alkyl, -C<sub>1-4</sub> alkyl-pyridyl, -C(O)CH<sub>2</sub>NH<sub>2</sub> and -CH<sub>2</sub>N(C<sub>1-4</sub> alkyl)<sub>2</sub>.

Another example of prodrug of the compound of formula (I) is a compound of the formula (I), wherein the carboxyl group is substituted with a group selected from C<sub>1-4</sub> alkyl, -CH<sub>2</sub>-C<sub>1-4</sub>alkyl-O-C(O)-C<sub>1-4</sub>alkyl, -CH<sub>2</sub>-C<sub>1-4</sub>alkyl-O-C(O)-N(C<sub>1-4</sub>alkyl)<sub>2</sub>, -CH<sub>2</sub>C(O)-N(C<sub>1-4</sub> alkyl)<sub>2</sub>, -CH<sub>2</sub>-C<sub>1-4</sub>alkyl-O-C(O)-O-C<sub>1-4</sub>alkyl, ethyl-OH and -CH<sub>2</sub>CO<sub>2</sub>H.

The compounds of the formula (I) of this invention can be administered via either the oral, parenteral or topical routes to mammals. In general, these compounds are most desirably administered to humans in doses ranging from 0.01 mg to 100 mg

per kg of body weight per day, although variations will necessarily occur depending upon the weight, sex and condition of the subject being treated, the disease state being treated and the particular route of administration chosen. However, a dosage level that is in the range of from 0.01 mg to 10 mg per kg of body weight per day, single or 5 divided dosage is most desirably employed in humans for the treatment of abovementioned diseases.

The compounds of the present invention may be administered alone or in combination with pharmaceutically acceptable carriers or diluents by either of the above routes previously indicated, and such administration can be carried out in single 10 or multiple doses. More particularly, the novel therapeutic agents of the invention can be administered in a wide variety of different dosage forms, i.e., they may be combined with various pharmaceutically acceptable inert carriers in the form of tablets, capsules, lozenges, trochees, hard candies, powders, sprays, creams, salves, suppositories, jellies, gels, pastes, lotions, ointments, aqueous suspensions, injectable solutions, elixirs, 15 syrups, and the like. Such carriers include solid diluents or fillers, sterile aqueous media and various nontoxic organic solvents, etc. Moreover, oral pharmaceutical compositions can be suitably sweetened and/or flavored. In general, the therapeutically-effective compounds of this invention are present in such dosage forms at concentration levels ranging 5% to 70% by weight, preferably 10% to 50% by 20 weight.

For oral administration, tablets containing various excipients such as microcrystalline cellulose, sodium citrate, calcium carbonate, dipotassium phosphate and glycine may be employed along with various disintegrants such as starch and preferably corn, potato or tapioca starch, alginic acid and certain complex silicates, 25 together with granulation binders like polyvinylpyrrolidone, sucrose, gelatin and acacia. Additionally, lubricating agents such as magnesium stearate, sodium lauryl sulfate and talc are often very useful for tabletting purposes. Solid compositions of a similar type may also be employed as fillers in gelatine capsules; preferred materials in this connection also include lactose or milk sugar as well as high molecular weight 30 polyethylene glycols. When aqueous suspensions and/or elixirs are desired for oral administration, the active ingredient may be combined with various sweetening or

flavoring agents, coloring matter or dyes, and, if so desired, emulsifying and/or suspending agents as well, together with such diluents as water, ethanol, propylene glycol, glycerin and various combinations thereof.

For parenteral administration, solutions of a compound of the present invention  
5 in either sesame or peanut oil or in aqueous propylene glycol may be employed. The aqueous solutions should be suitably buffered (preferably pH>8) if necessary and the liquid diluent first rendered isotonic. These aqueous solutions are suitable for intravenous injection purposes. The oily solutions are suitable for intra-articular, intra-muscular and subcutaneous injection purposes. The preparation of all these  
10 solutions under sterile conditions is readily accomplished by standard pharmaceutical techniques well-known to those skilled in the art. Additionally, it is also possible to administer the compounds of the present invention topically when treating inflammatory conditions of the skin and this may preferably be done by way of creams, jellies, gels, pastes, ointments and the like, in accordance with standard  
15 pharmaceutical practice.

The compounds of formula (I) may also be administered in the form of suppositories for rectal or vaginal administration of the active ingredient. These compositions can be prepared by mixing the active ingredient with a suitable non-irritating excipient which is solid at room temperature (for example, 10 °C to 32 °C)  
20 but liquid at the rectal temperature and will melt in the rectum or vagina to release the active ingredient. Such materials are polyethylene glycols, cocoa butter, suppository and wax.

For buccal administration, the composition may take the form of tablets or lozenges formulated in conventional manner.

25 *Combination with Other Drugs:*

Compounds of Formula I would be useful for, but not limited to, the treatment of inflammation in a subject, and for treatment of other inflammation-associated disorders, such as, as an analgesic in the treatment of pain and headaches, or as an antipyretic for the treatment of fever. For example, combinations of the invention would be useful  
30 to treat arthritis, including but not limited to rheumatoid arthritis, spondyloarthropathies, gouty arthritis, osteoarthritis, systemic lupus erythematosus and juvenile arthritis.

Such combinations of the invention would be useful in the treatment of asthma, bronchitis, inmenstrual cramps, tendinitis, bursitis, and skin related conditions such as psoriasis, eczema, burns and dermatitis. Combinations of the invention also would be useful to treat gastrointestinal conditions such as inflammatory bowel disease.

5 Crohn's disease, gastritis, irritable bowel syndrome and ulcerative colitis and for the prevention of colorectal cancer. Combinations of the invention would be useful in creating inflammation in such diseases as vascular diseases, migraine headaches, periarteritis nodosa, thyroiditis, aplastic anemia, Hodgkin's disease, sclerodoma, rheumatic fever, type I diabetes, myasthenia gravis, multiple sclerosis, sarcoidosis,

10 nephrotic syndrome, Behcet's syndrome, polymyositis, gingivitis, hypersensitivity, Conjunctivitis, swelling occurring after injury, myocardial ischemia, and the like. The combinations would also be useful for the treatment of certain central nervous system disorders such as Alzheimer's disease and dementia. The combinations of the invention are useful as anti-inflammatory agents, such as for the treatment of arthritis,

15 with the additional benefit of having significantly less harmful side effects. These compositions would also be useful in the treatment of allergic rhinitis, respiratory distress syndrome, endotoxin shock syndrome, atherosclerosis and central nervous system damage resulting from stroke, ischemia and trauma.

Compounds of formula (I) will be useful as a partial or complete substitute for conventional NSAID's in preparations wherein they are presently co-administered with other agents or ingredients. Thus, the invention encompasses pharmaceutical compositions for treating COX-2 mediated diseases as defined above comprising a non-toxic therapeutically effective amount of the compound of formula (I) and one or more ingredients such as another pain reliever including acetaminophen or phenacetin; a potentiator including caffeine; an H<sub>2</sub>-antagonist, aluminom or magnesium hydroxide, simethicone, a decongestant including phenylephrine, phenylproanolamine, psuedophedrine, oxymetazoline, ephinephrine, naphazoline, xylometazoline, propylhexedrine, or levodesoxyephedrine; an antitussive including codeine, hydrocodone, caramiphen, carbetapentane, or dextromethorphan; a prostaglandin including misoprostol, enprostil, rioprostil, ornoprostol or rosaprostol; a diuretic; a sedating or non-sedating antihistamine; anticancer agents such as angiostatin and

endostatin; anti-Alzheimers such as Doepezil and Tacrine hydrochloride; and TNF alpha inhibitors such as Etanercept.

These cyclooxygenase inhibitors can further be used in combination with a nitric oxide inhibitors disclosed in WO 96/28145.

5 Also, the invention encompasses pharmaceutical compositions for treating COX-2 mediated diseases as defined above comprising a non-toxic therapeutically effective amount of the compound of formula (I) and one or more anti-ulcer agent and/or prostaglandins, which are disclosed in WO 97/11701.

10 The useful prostaglandins include misoprostol, plus-minus methyl 11 $\alpha$ , 16-dihydroxy-16-methyl-9-oxoprostan-13E-en-1-oate; enisoprost and methyl-7-[2B-[6-(1-cyclopenten-1-yl)-4-hydroxy-4-methyl-1E, 5E-hexadienyl]-3 $\alpha$ -hydroxy-5-oxo 1R, 1 $\alpha$ -cyclopentyl]-4Z-heptenoate. Prostaglandins within the scope of the invention also include arbabrostonil, enprostil, rioprostol, nocloprost, mexiprostol, ornoprostol, dimoxaprostan, tiprostanide and rosaprostanol.

15 The present compounds may also be used in co-therapies, partially or completely in place of other conventional antiinflammatories, such as together with steroids, 5-lipoxygenase inhibitors, LTB<sub>4</sub> antagonists and LTA<sub>4</sub> hydrolase inhibitor's.

An example of LTB<sub>4</sub> is disclosed in WO97/29774. Suitable LTB<sub>4</sub> inhibitors include, among others, ebselen, Bayer Bay-x-1005, Ciba Geigy compound CGS 25019C, Leo Denmark compound ETH-615, Lilly compound LY-293111, Ono compound ONO-4057, Terumo compound TMK-688, Lilly compounds LY-213023, 264086 and 292728, Ono compound ONO-LB457, Searle compound SC-S3218 calcitrol, Lilly compounds LY-210073, LY223982, LY233469, and LY255283, Ono compound ONO-LB-448, Searle compounds SC-41930, SC-50605 and SC-51146, and 25 SK&F compound SKF-104493. Preferably, the LTB<sub>4</sub> inhibitors are selected from ebselen, Bayer Bay-x-1005, Ciba Geigy compound CGS-25019C, Leo Denmark compound ETH-61S, Lilly compound LY-293111, Ono compound ONO-4057 and Terumo compound TMK-688.

An example of 5-LO inhibitors is disclosed in WO97/29776. Suitable 5-LO 30 inhibitors include, among others, masoprocol, tenidap, zileuton, pranlukast, tepronolin, rilopirox, flezelastine hydrochloride, enazadrem phosphate and bunaprolast.

An example of LTA<sub>4</sub> hydrolase inhibitors is disclosed in WO97/29774. Suitable LTA<sub>4</sub> hydrolase inhibitors include, among others, Rhone-Poulenc Rorer RP-64966.

The administration of the present invention may be for either prevention or 5 treatment purposes. The methods and compositions used herein may be used alone or in conjunction with additional therapies known to those skilled in the art in the prevention or treatment of angiogenesis. Alternatively, the methods and compositions described herein may be used as adjunct therapy. By way of example, the cyclooxygenase-2 inhibitor may be administered alone or in conjunction with other 10 antineoplastic agents or other growth inhibiting agents or other drugs or nutrients.

There are large numbers of antineoplastic agents available in commercial use, in clinical evaluation and in pre-clinical development, which could be selected for treatment of angiogenesis by combination drug chemotherapy. Such antineoplastic agents fall into several major categories, namely, antibiotic-type agents, alkylating 15 agents, antimetabolite agents, hormonal agents, immunological agents, interferon-type agents and a category of miscellaneous agents. Alternatively, other anti-neoplastic agents , such as metallocmatrix proteases inhibitors (MMP) , such as MMP-13 inhibitors including batistat, marimastat. Agouron Pharmaceuticals AG-3340, and Roche R0-32-3555, or alpha,beta,inhibitors may be used.

20 A first family of antineoplastic agents which may be used in combination with a selective cyclooxygenase-2 inhibitor consists of antimetabolite-type antineoplastic agents. Suitable antimetabolite antineoplastic agents may be selected from the group consisting of 5-FU-fibrinogen, acanthifolic acid, aminothiadiazole, brequinar sodium, carmofur, Ciba-Geigy CGP-30694, cyclopentyl cytosine, cytarabine phosphate stearate, 25 cytarabine conjugates, Lilly DATHF, Merrel Dow DDFC, dezaguanine, dideoxycytidine, dideoxyguanosine, didox, Yoshitomi DMDC, doxifluridine, Wellcome EHNA, Merck & Co. EX-015, fazarabine, floxuridine, fludarabine phosphate, 5-fluorouracil, N-(2'-furanidyl)-5-fluorouracil, Daiichi Seiyaku F0-152, isopropyl pyrrolizine, Lilly LY-188011, Lilly LY-264618, methobenzaprim, 30 methotrexate, Wellcome MZPES. norspermidine, NCI NSC-127716, NCI NSC-264880, NCI NSC-39661, NCI NSC-612567, Warner-Lambert PALA, pentostatin,

piritrexim, plicamycin, Asahi Chemical PL-AC, Takeda TAC-788, thioguanine, tiazofurin, Erbamont TIF, trimetrexate, tyrosine kinase inhibitors, tyrosine protein kinase inhibitors, Taiho UFT and uricytin.

A second family of antineoplastic agents which may be used in combination with a selective cyclooxygenase-2 inhibitor consists of alkylating-type antineoplastic agents. Suitable alkylating-type antineoplastic agents may be selected from the group consisting of Shionogi 254-S, aldo-phosphamide analogues, altretamine, anaxirone, Boehringer Mannheim BBR-2207, bestabucil, budotitane, Wakunaga CA-I02, carboplatin, carmustine, Chinoin-139, Chinoin-153, chlorambucil, cisplatin, cyclophosphamide, American Cyanamid CL-286558, Sanofi CY-233, cyplatate, Degussa D-19-384, Sumimoto DACHP(Myr)2, diphenylspiromustine, diplatinum cytostatic, Erba distamycin derivatives, Chugai DWA-2114R, ITI E09, elmustine, Erbamont FCE-24517, estramustine phosphate sodium, fotemustine, Unimed G-6-M, Chinoin GYKI-17230, hepsul-fam, ifosfamide, iproplatin, Iomustine, mafosfamide, mitolactol, Nippon Kayaku NK-121, NCI NSC-264395, NCI NSC-342215, oxaliplatin, Upjohn PCNU, prednimustine, Proter PTT-II9, ranimustine, semustine, SmithKline SK&F-I01772, Yakult Honsha SN-22, spiromus-tine, Tanabe Seiyaku TA-077 tauromustine, temozolomide, teroxirone, tetraplatin and trimelamol.

A third family of antineoplastic agents which may be used in combination with a selective cyclooxygenase-2 inhibitor consists of antibiotic-type antineoplastic agents. Suitable antibiotic-type antineoplastic agents may be selected from the group consisting of Taiho 4181-A, aclarubicin, actinomycin D, actinoplanone, Erbamont ADR-456, aeroplysinin derivative, Ajinomoto AN-201-II, Ajinomoto AN-3, Nippon Soda anisomycins, anthracycline, azino-mycin-A, bisucaberin, Bristol-Myers BI-6859, Bristol-Myers BMY-25067, Bristol-Myers BMY-25551, Bristol-Myers BMY-26605, Bristol-Myers BMY-27557, Bristol-Myers BMY-28438, bleomycin sulfate, bryostatin-1, Taiho C-I027, calichemycin, chromoximycin, dactinomycin, daunorubicin, Kyowa Hakko DC-I02, Kyowa Hakko DC-79, Kyowa Hakko DC-88A, Kyowa Hakko DC89-Al, Kyowa Hakko DC92-B, ditrisarubicin B, Shionogi DOB-41, doxorubicin, doxorubicin-fibrinogen, elsamicin-A, epirubicin, erbstatin, esorubicin, esperamicin-A1, esperamicin-Alb, Erbamont FCE-21954, Fujisawa FK-973, fostriecin, Fujisawa FR-

- 900482, glidobactin, gregatin-A, grincamycin, herbimycin, idarubicin, illudins, kazusamycin, kesarirhodins, Kyowa Hakko KM-5539, Kirin Brewery KRN-8602, Kyowa Hakko KT-5432, Kyowa Hakko KT-5594, Kyowa Hakko KT-6149, American Cyanamid LL-D49194, Meiji Seika ME 2303, menogaril, mitomycin, mitoxantrone,
- 5 SmithKline M-TAG, neoenactin, Nippon Kayaku NK-313, Nippon Kayaku NKT-OI, SRI International NSC-357704, oxalysine, oxaunomycin, peplomycin, pilatin, pirarubicin, porothramycin, pyrindamycin A, Tobishi RA-I, rapamycin, rhizoxin, roedorubicin, sibanomicin, siwenmycin, Sumitomo SM-5887, Snow Brand SN-706, Snow Brand SN-07, sorangicin-A, sparsomycin, SS Pharmaceutical SS-21020, SS
- 10 Pharmaceutical SS-7313B, SS Pharmaceutical SS-9816B, steffimycin B, Taiho 4181-2, talisomycin, Takeda TAN-868A, terpentecin, thrazine, tricrozarin A, Upjohn U-73975, Kyowa Hakko UCN-I0028A, Fujisawa WF-3405, Yoshitomi Y-2S024 and zorubicin.

A fourth family of antineoplastic agents which may be used in combination with the selective cyclooxygenase-2 inhibitor consists of a miscellaneous family of antineoplastic agents selected from the group consisting of alpha-carotene, alpha-difluoromethyl-arginine, acitretin, Biotec AD-5, Kyorin AHC-52, alstonine, amonafide, amphethinile, amsacrine, Angiostat, ankinomycin, anti-neoplaston AIO, antineoplaston A2, antineoplaston A3, antineoplaston A5, antineoplaston AS2-1, Henkel APD, aphidicolin glycinate, asparaginase, Avarol, baccharin, batracylin, benfluron, benzotript, Ipsen-Beaufour BIM-23015, bisantrene, Bristol-Myers BMY-40481, Vestar boron-IO, bromofosfamide, Wellcome BW-502, Wellcome BW-773, caracemide, carmethizole hydrochloride, Ajinomoto CDAF, chlorsulfaquinoxalone, Chemes CHX-2053, Chemex CHX-1OO, Warner-Lambert CI-921, Warner-Lambert CI-937, Warner-Lambert CI-941, Warner-Lambert CI-958, clanfenur, claviridenone, ICN compound 1259, ICN compound 4711, Contracan, Yakult Honsha CPT-11, crisnatol, curaderm, cytochalasin B, cytarabine, cytotoxicity, Merz D-609, DABIS maleate, dacarbazine, datelliptinium, didemnin-B, dihaematoporphyrin ether, dihydrolenperone, dinaline, distamycin, Toyo Pharmar DM-341, Toyo Pharmar DM-75, Daiichi Seiyaku DN-9693, elliprin, elliptinium acetate, Tsumura EPMTC, ergotamine, etoposide, etretinate, fenretinide, Fujisawa FR-57704, gallium nitrate, genkwadaphnin, Chugai GLA-43, Glaxo GR-63178, grifolan NMF-5N, hexadecylphosphocholine, Green Cross H0-221,

- homoharringtonine, hydroxyurea, BTG ICRF-187, ilmofosine, isoglutamine, isotretinoin. Otsuka JI-36, Ramot K-477, Otsuak K-76COONa, Kureha Chemical K-AM, MECT Corp KI-8110, American Cyanamid L-623, leukoregulin, ionidamine, Lundbeck LU-23-II2, Lilly LY-186641, NCI (US) MAP, marycin, Merrel Dow MDL-5 27048, Medco MEDR-340, merbarone, merocyanine derivatives, methylanilinoacridine, Molecular Genetics MGI-136, minactivin, mitonafide, mitoquidone, mepidamol, motretinide, Zenyaku Kogyo MST-16, N-(retinoyl)amino acids, Nissin Flour Milling N-021, N-acylated-dehydroalanines, nafazatrom, Taisho NCU-190, nocodazole derivative, Normosang, NCI NSC-145813, NCI NSC-361456, NCI NSC-604782, NCI 10 NSC-95580, octreotide, Ono ON0-112, oquizanocene, Akzo Org-I0172, pancratistatin, pazelliptine, Warner-Lambert PD-II1707, Warner-Lambert PD-115934, Warner-Lambert PD-131141, Pierre Fabre PE-1001, ICRT peptide D, piroxantrone, polyhaematoporphyrin, polypreic acid, Efamol porphyrin, probimane, procarbazone, proglurnide, Invitron protease nexin I, Tobishi RA-700, razoxane, Sapporo Breweries 15 RBS, restrictin-P, retelliptine, retinoic acid, Rhone-Poulenc RP-49532, Rhone-Poulenc RP-56976, SmithKline SK&F-I04864, Sumitomo SM-108, Kuraray SMANCS, SeaPharm SP-I0094, spatol, spirocyclopropane derivatives, spirogermanium, Unimed SS Pharmaceutical SS-554, strypoldinone, Stypoldione, Suntory SUN 0237, Suntory SUN 2071, superoxide dismutase, Toyama T-506, Toyama T-680, taxol, Temm 11 20 0303, teniposide, thaliblastine, Eastman Kodak TJB-29, tocotrienol, Topostin, Temm TT-82, kyowa Hakko UCN-O1, Kyowa Hakko UCN-I028, ukrain, Eastman Kodak USB-006, vinblastine sulfate, vincristine, vindesine, vinestramide, vinorelbine, vintripotol, vinzolidine, withanolides and Yamanouchi YM-534.

Examples of radioprotective agents which may be used in the combination 25 chemotherapy of this invention are AD-5, adchnon, amifostine analogues, detox, dimesna, I-102, MN-159, N-acylated-dehydroalanines, TGF-Genentech, tiprotimod, amifostine, WR-I51327, FUT-187, ketoprofen transdermal, naburnetone, superoxide dismutase (Chiron) and superoxide dismutase Enzon.

Methods for preparation of the antineoplastic agents described above may be 30 found in the literature. Methods for preparation of doxorubicin, for example, are described in U.S. Patents No. 3,590,028 and No. 4,012,448. Methods for preparing

metallomatrix protease inhibitors are described in EP 780386, WO97/20824. WO96/15096. Methods for preparing SOD mimics are described in EP 524,101. Methods for preparing alpha,beta, inhibitors are described in W097/08174.

In addition, the selective COX-2 inhibitor may be administered in conjunction  
5 with other antiinflammatory agents for maximum safety and efficacy, including  
NSAID's, selective COX-1 inhibitors and inhibitors of the leukotriene pathway,  
including 5-lipoxygenase inhibitors. Examples of NSAID's include indomethacin,  
naproxen, ibuprofen, salicylic acid derivatives such as aspirin, diclofenac, ketorolac,  
piroxicam, meloxicam, mefenamic acid, sulindac, tolmetin sodium, zomepirac,  
10 fenoprofen, phenylbutazone, oxyphenbutazone, nimesulide, zaltoprofen and letodolac.

**Method for assessing biological activities:**

The activity of the compounds of the formula (I) of the present invention was demonstrated by the following assays.

*In vitro assays*

15 *Human cell based COX-1 assay*

Human peripheral blood obtained from healthy volunteers was diluted to 1/10 volume with 3.8% sodium citrate solution. The platelet-rich plasma immediately obtained was washed with 0.14 M sodium chloride containing 12 mM Tris-HCl (pH 7.4) and 1.2 mM EDTA. Platelets were then washed with platelet buffer (Hanks buffer (Ca free) containing 0.2% BSA and 20 mM Hepes). Finally, the human washed platelets (HWP) were suspended in platelet buffer at the concentration of 2.85  $\times 10^8$  cells/ml and stored at room temperature until use. The HWP suspension (70  $\mu$ l aliquots, final 2.0  $\times 10^7$  cells/ml) was placed in a 96-well U bottom plate and 10  $\mu$ l aliquots of 12.6 mM CaCl<sub>2</sub> added. Platelets were incubated with A23187 (final 10  $\mu$ M, Sigma) with test compound (0.1 - 100  $\mu$ M) dissolved in DMSO (final concentration; less than 0.01%) at 37 °C for 15 min. The reaction was stopped by addition of EDTA (final 7.7 mM) and TxB<sub>2</sub> in the supernatant quantitated by using a radioimmunoassay kit (Amersham) according to the manufacturer's procedure.

*Human cell based COX-2 assay*

30 Inhibition of COX-2 activity after induction of COX-2 by hIL-1 $\beta$

The human cell based COX-2 assay was carried out as previously described

(Moore *et al.*, *Inflamm. Res.*, **45**, 54, 1996). Confluent human umbilical vein endothelial cells (HUVECs, Morinaga) in a 96-well U bottom plate were washed with 100 µl of RPMI1640 containing 2% FCS and incubated with hIL-1 $\beta$  (final concentration 300 U/ml, R & D Systems) at 37 °C for 24 hr. After washing, the 5 activated HUVECs were stimulated with A23187 (final concentration 30 µM) in Hanks buffer containing 0.2% BSA, 20 mM Hepes and test compound (0.1 nM - 100 µM) dissolved in DMSO (final concentration; less than 0.01%) at 37 °C for 15 min. 6-Keto-PGF1 $\alpha$ , stable metabolite of PGJ2, in the supernatant was quantitated after adequate dilution by using a radioimmunoassay kit (Amersham) according to the 10 manufacturer's procedure.

Inhibition of COX-2 during the induction phase

Confluent human umbilical vein endothelial cells (HUVECs, Morinaga) in a 96-well U bottom plate were washed with 100 µl of RPMI1640 containing 2% FCS and test compound (0.1 nM - 100 µM) dissolved in DMSO (final concentration; less 15 than 0.01%), and incubated with hIL-1 $\beta$  (final concentration 300 U/ml, R & D Systems) at 37 °C for 24 hr. After washing, the HUVECs were stimulated with A23187 (final concentration 30 µM) in Hanks buffer containing 0.2% BSA and 20 mM Hepes at 37 °C for 15 min. 6-Keto-PGF1 $\alpha$ , a stable metabolite of PGJ2, in the supernatant was quantitated after adequate dilution by using a radioimmunoassay kit 20 (Amersham) according to the manufacturer's procedure.

*In vivo assays*

*Carrageenan induced foot edema in rats*

Male Sprague-Dawley rats (5 weeks old, Charles River Japan) were fasted overnight. A line was drawn using a marker above the ankle on the right hind paw 25 and the paw volume (V0) was measured by water displacement using a plethysmometer (Muromachi). Animals were given orally either vehicle (0.1% methyl cellulose or 5% Tween 80) or a test compound (2.5 ml per 100 g body weight). One hour later, the animals were then injected intradermally with  $\lambda$ -carrageenan (0.1 ml 30 of 1% w/v suspension in saline, Zushikagaku) into right hind paw (Winter *et al.*, *Proc Soc. Exp. Biol. Med.*, **111**, 544, 1962; Lombardino *et al.*, *Arzneim. Forsch.*, **25**, 1629, 1975) and three hours later, the paw volume (V3) was measured and the increase in

volume ( $V_3 - V_0$ ) calculated. Since maximum inhibition attainable with classical NSAIDs is 60-70%, ED<sub>30</sub> values were calculated.

*Gastric ulceration in rats*

The gastric ulcerogenicity of test compound was assessed by a modification of  
5 the conventional method (Ezer *et al.*, *J. Pharm. Pharmacol.*, **28**, 655, 1976; Cashin *et*  
*al.*, *J. Pharm. Pharmacol.*, **29**, 330 - 336, 1977). Male Sprague-Dawley rats (5 weeks  
old, Charles River Japan), fasted overnight, were given orally either vehicle (0.1%  
methyl cellulose or 5% Tween 80) or a test compound (1 ml per 100 g body weight).  
Six hours after, the animals were sacrificed by cervical dislocation. The stomachs  
10 were removed and inflated with 1% formalin solution (10 ml). Stomachs were  
opened by cutting along the greater curvature. From the number of rats that showed  
at least one gastric ulcer or haemorrhaging erosion (including ecchymosis), the  
incidence of ulceration was calculated. Animals did not have access to either food or  
water during the experiment.

15 **Data Analysis**

Statistical program packages, SYSTAT (SYSTAT, INC.) and StatView  
(Abacus Concepts, Inc.) for Macintosh were used. Differences between test  
compound treated group and control group were tested for using ANOVA. The IC<sub>50</sub>  
(ED<sub>30</sub>) values were calculated from the equation for the log-linear regression line of  
20 concentration (dose) versus percent inhibition.

Some compounds prepared in the Working Examples as described herein after  
were tested by these methods, and showed IC<sub>50</sub> values of 0.001  $\mu\text{M}$  to 10  $\mu\text{M}$  with  
respect to inhibition of COX-2.

Also, the above-mentioned most preferred compounds were tested by these  
25 methods, and showed IC<sub>50</sub> values of 0.001  $\mu\text{M}$  to 0.5  $\mu\text{M}$  with respect to inhibition of  
COX-2.

COX-2 selectivity can be determined by ratio in terms of IC<sub>50</sub> value of COX-1  
inhibition to COX-2 inhibition. In general, it can be said that a compound showing a  
COX-1/COX-2 inhibition ratio of more than 2 has good COX-2 selectivity.

30 Some compounds prepared in Examples showed COX-1/COX-2 inhibition ratio  
of more than 10.

The following examples contain detailed descriptions of the methods of the preparation of compounds of formula (I). These detailed descriptions fall within the scope of the invention and serve to exemplify the above described general synthetic procedures which form part of the invention. These detailed descriptions are 5 presented for illustrative purposes only and are not intended to restrict the scope of the present invention.

## EXAMPLES

The invention is illustrated in the following non-limiting examples in which, unless stated otherwise: all operations were carried out at room or ambient temperature. 10 that is, in the range of 18-25 °C; evaporation of solvent was carried out using a rotary evaporator under reduced pressure with a bath of up to 60 °C; reactions were monitored by thin layer chromatography (tlc) and reaction times are given for illustration only; melting points (m.p.) given are uncorrected (polymorphism may result in different melting points); structure and purity of all isolated compounds were assured by at least 15 one of the following techniques: tlc (Merck silica gel 60 F-254 precoated plates), mass spectrometry, nuclear magnetic resonance (NMR) or microanalysis. Yields are given for illustrative purposes only. Flash column chromatography was carried out using Merck silica gel 60 (230-400 mesh ASTM). Low-resolution mass spectral data (LI) were obtained on a Automass 120 (JEOL) mass spectrometer. Low-resolution mass 20 spectral data (ESI) were obtained on a Quattro II (Micromass) mass spectrometer. NMR data was determined at 270 MHz (JEOL JNM-LA 270 spectrometer) using deuterated chloroform (99.8% D) or dimethylsulfoxide (99.9% D) as solvent unless indicated otherwise, relative to tetramethylsilane (TMS) as internal standard in parts per million (ppm); conventional abbreviations used are: s = singlet, d = doublet, t 25 triplet, q = quartet, m = multiplet, br = broad, etc.

### EXAMPLE 1

#### ETHYL (2-BENZOYL-6-CHLORO-1H-INDOL-3-YL)ACETATE

##### STEP 1. Ethyl *trans*-4-chloro-2-nitrocinnamate

To a suspension of sodium hydride (60% w/w dispersion in mineral oil, 4.4 g. 30 0.11 mol) in THF (150 ml) was added dropwise a solution of triethyl phosphonoacetate (25.0 g, 0.11 mol) in THF (50 ml) at room temperature. After stirring for 1 h, a

solution of 4-chloro-2-nitrobenzaldehyde (19.0 g, 0.10 mol) in THF (50 ml) was added. After stirring for an additional 1 h, saturated aqueous ammonium chloride (50 ml) was added and the resulting mixture was extracted with ethyl acetate (300 ml x 2). The combined organic extracts were dried ( $\text{MgSO}_4$ ) and concentrated to give 27 g (quant.) of the title compound as brown solids.

5       $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.04 (1H, d,  $J=15.8$  Hz), 8.03 (1H, d,  $J=1.8$  Hz), 7.64-7.58 (2H, m), 6.36 (1H, d,  $J=15.8$  Hz), 4.30 (2H, q,  $J=7.0$  Hz), 1.35 (3H, t,  $J=7.0$  Hz).

STEP 2. Ethyl *trans*-2-amino-4-chlorocinnamate

A mixture of ethyl *trans*-4-chloro-2-nitrocinnamate (step 1, 27.0 g, 0.11 mol) 10 and sodium hydrosulfite (92 g, 0.53 mol) in  $\text{THF-H}_2\text{O}$  (1:1, 500 ml) was stirred at room temperature for 1h. Saturated aqueous sodium bicarbonate (300 ml) was then added and the mixture was extracted with ethyl acetate (300 ml x 2). The combined organic extracts were dried ( $\text{MgSO}_4$ ) and concentrated to give 16.7 g (67%) of the title compound as yellow solids.

15       $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 7.72 (1H, d,  $J=15.8$  Hz), 7.27 (1H, d,  $J=8.4$  Hz), 6.78-6.68 (2H, m), 6.31 (1H, d,  $J=15.8$  Hz), 4.27 (2H, q,  $J=7.0$  Hz), 1.33 (3H, t,  $J=7.0$  Hz).

STEP 3. Ethyl *trans*-4-chloro-2-formamidocinnamate

A mixture of acetic anhydride (20 ml) and formic acid (10 ml) was heated at 60 °C for 2 h. After cooling to 0 °C, a solution of ethyl *trans*-2-amino-4-chlorocinnamate 20 (step 2, 15.5 g, 0.069 mol) in THF (80 ml) was carefully added. The resulting mixture was allowed to warm to room temperature. After stirring overnight, the mixture was concentrated and the precipitates were collected by filtration. The solids were washed with hexane to give 9.6 g (55%) of the title compound.

25       $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 9.40-9.15 (1H, m), 8.51-8.40 (1H, m), 8.10-7.80 (2H, m), 7.60-7.47 (1H, m), 7.28-7.12 (1H, m), 6.40 (1H, d,  $J=15.8$  Hz), 4.25 (2H, q,  $J=7.3$  Hz), 1.34 (3H, t,  $J=7.3$  Hz).

STEP 4. Ethyl *trans*-4-chloro-2-isocyanocinnamate

To a solution of triphenylphosphine (5.3 g, 20 mmol) in dichloromethane (80 ml) cooled to 0 °C was added dropwise a solution of triphosgene (2.0 g, 6.7 mmol) in 30 dichloromethane (20 ml). The ice-bath was removed and the resulting mixture stirred

at room temperature for 10 min. The mixture was then cooled to 0 °C and a solution of ethyl *trans*-4-chloro-2-formamidocinnamate (step 3, 5.2 g, 0.020 mol) in dichloromethane (80 ml) was added. The mixture was allowed to warm to room temperature overnight, and then concentrated. The residue was partitioned between 5 water (80 ml) and ethyl acetate (100 ml), the aqueous layer separated and extracted with ethyl acetate (100 ml). The combined organic extracts were dried ( $\text{MgSO}_4$ ), solvent removed by evaporation and the crude product was purified by flash column chromatography eluting with ethyl acetate/hexane (1:6) to afford 3.9 g (83 %) of the title compound as white solids.

10  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 7.89 (1H, d,  $J=16.1$  Hz), 7.60 (1H, d,  $J=8.8$  Hz), 7.45 (1H, d,  $J=1.8$  Hz), 7.42 (1H, dd,  $J=1.8, 8.8$  Hz), 6.52 (1H, d,  $J=16.1$  Hz), 4.30 (2H, q,  $J=7.0$  Hz), 1.35 (3H, t,  $J=7.0$  Hz).

**STEP 5. Ethyl (2-benzoyl-6-chloro-1H-indol-3-yl)acetate**

A mixture of ethyl *trans*-4-chloro-2-isocyanocinnamate (step 4, 1.2 g, 5.1 mmol), tributyltin hydride (1.6 g, 5.6 mmol) and AIBN (43 mg, 0.26 mmol) in acetonitrile (30 ml) was heated at 100 °C. After 1 h tetrakis(triphenylphosphine)palladium (580 mg, 0.50 mmol) and benzoyl chloride (0.68 ml, 5.6 mmol) were added and the mixture was heated for a further 17 h. The mixture was cooled and poured into 2N aqueous HCl (50 ml) and extracted with diethyl ether (80 ml x 2). The combined organic extracts were washed with saturated aqueous potassium fluoride (50 ml) and dried ( $\text{MgSO}_4$ ). After removal of solvent, the crude product was purified by flash column chromatography eluting with ethyl acetate/hexane (1:5) to afford 0.43 g (25 %) of the title compound as white solids.  
m.p.: 160-163 °C.

25  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.94 (1H, br s), 7.82-7.75 (2H, m), 7.67-7.47 (4H, m), 7.37 (1H, d,  $J=1.8$  Hz), 7.13 (1H, dd,  $J=1.8, 8.4$  Hz), 4.11 (2H, q,  $J=7.3$  Hz), 3.78 (2H, s), 1.22 (3H, t,  $J=7.3$  Hz).

**EXAMPLE 2**

**(2-BENZOYL-6-CHLORO-1H-INDOL-3-YL)ACETIC ACID**

30 **METHOD A**

To a solution of ethyl (2-benzoyl-6-chloro-1H-indol-3-yl)acetate (Example 1,

380 mg, 0.11 mmol) in ethanol (15 ml) was added 2N aqueous KOH (5 ml). After heating at 80 °C for 1 h, the mixture was cooled and concentrated, and then 2N aqueous HCl (15 ml) added carefully. The mixture was extracted with diethyl ether (50 ml x 2), the combined organic extracts dried ( $MgSO_4$ ) and concentrated. The residual solids were recrystallized from ethyl acetate/hexane to afford 60 mg (17%) of the title compound as pale yellow solids.

m.p.: 183-186 °C.

IR (KBr)  $\nu$ : 1700, 1610, 1520, 1425, 1330, 1000  $cm^{-1}$ .

$^1H$ -NMR (DMSO-d<sub>6</sub>)  $\delta$ : 12.26 (1H, br s), 11.76 (1H, s), 7.77-7.66 (4H, m), 7.62-7.54 (2H, m), 7.48 (1H, d,  $J$ =1.8 Hz), 7.13 (1H, dd,  $J$ =1.8, 8.7 Hz), 3.80 (2H, s).

#### METHOD B

##### STEP 1. 6-Chloro-1-(phenylsulfonyl)indole

A mixture of 6-chloroindole (Y. Watanabe et al., *J. Org. Chem.*, 1990, **55**, 580, 36.2 g, 0.24 mol), tetrabutylammonium hydrogen sulfate (8.1 g, 0.024 mol) and 15 50 % aqueous KOH (160 ml) in benzene (500 ml) was stirred at room temperature for 10 min. The mixture was then cooled to 0 °C and a solution of benzenesulfonyl chloride in benzene (20 ml) was added. After stirring at room temperature for 3 h, the mixture was poured into water (200 ml), the organic layer separated and the aqueous layer extracted with diethyl ether (200 ml x 2). The combined organic extracts were 20 washed with brine (200 ml), dried ( $MgSO_4$ ) and concentrated. The residual solids were washed with ethanol (100 ml x 3) to give 58 g (83%) of the title compound as off-white solids.

$^1H$ -NMR (CDCl<sub>3</sub>)  $\delta$ : 8.02 (1H, s), 7.92-7.85 (2H, m), 7.60-7.40 (5H, m), 7.21 (1H, dd,  $J$ =1.8, 8.4 Hz), 6.62 (1H, d,  $J$ =3.6 Hz).

25 STEP 2. 6-chloro-2-benzoyl-1-(phenylsulfonyl)indole

To a stirred solution of 6-chloro-1-(phenylsulfonyl)indole (Step 1, 12.58 g, 43.0 mmol) in THF (270 ml) cooled to - 78 °C was added dropwise *tert*-butyllithium (32 ml, 52.0 mmol, 1.64 M in *n*-pentane) with keeping the internal temperature below - 65 °C. After stirring for 30 min. at -78 °C, this solution was transferred via cannula to a 30 solution of benzoyl chloride (6.0 ml, 52.0 mmol) in THF (30 ml) cooled to - 78 °C. The mixture was stirred for 1.5 h and then quenched with saturated ammonium

chloride (200 ml) at -78 °C and allowed to warm to room temperature. The aqueous layer was separated and neutralized with aqueous sodium carbonate, and then extracted with ethyl acetate (50 ml x 2). The combined organic extracts were washed with brine (50 ml), dried ( $\text{MgSO}_4$ ), and concentrated. Crystallization of the residue from diethyl ether/hexane (1:3) afforded the title compound as white solids (14.4 g, 85%).

$^1\text{H-NMR}(\text{CDCl}_3)\delta$ : 8.20 - 8.16 (1H, m), 8.14 - 8.06 (2H, m), 8.01 - 7.93 (2H, m), 7.66 - 7.47 (7H, m), 7.29 (1H, dd,  $J=1.7$ , 8.5Hz), 6.89 (1H,  $J=0.7$ Hz).

STEP 3. 2-Benzoyl-6-chloroindole

A mixture of 2-benzoyl-6-chloro-1-(phenylsulfonyl)indole (step 2, 48 g, 0.12 mol) and potassium carbonate (80 g, 0.58 mol) in THF-MeOH-H<sub>2</sub>O (4:2:1, 1100 ml) was heated at reflux temperature overnight. After removal of solvent, the residue was extracted with diethyl ether (300 ml x 2) and dried ( $\text{MgSO}_4$ ). Removal of solvent gave the crude product as pale brown solids. Recrystallization from ethyl acetate afforded 20 g (65%) of the title compound as white solids.

15 m.p.: 206-207 °C.

$^1\text{H-NMR}(\text{CDCl}_3)\delta$ : 9.31 (1H, br s), 8.01-7.95 (2H m), 7.68-7.47 (5H, m), 7.17-7.11 (2H, m).

STEP 4. Diethyl  $\alpha$ -acetoxy-(2-benzoyl-6-chloro-1H-indol-3-yl)malonate

A mixture of 2-benzoyl-6-chloroindole (step 3, 4.0 g, 16 mmol), manganese(III) acetate dihydrate (13 g, 48 mmol), diethyl malonate (14 g, 80 mmol) and sodium acetate (6.6 g, 80 mmol) in acetic acid (150 ml) was heated at 80 °C with stirring for 2 h. Manganese(III) acetate dihydrate (3 g, 11 mmol) was added and heating was continued for an additional 2 h. The mixture was cooled and brine (200 ml) was added. The resulting mixture was extracted with diethyl ether (200 ml x 2) and the combined organic extracts dried ( $\text{MgSO}_4$ ) and concentrated. The residue was purified by flash column chromatography eluting with ethyl acetate/hexane (1:3) to afford 5.2 g (69 %) of the title compound as yellow solids.

m.p.: 141-144 °C.

$^1\text{H-NMR}(\text{CDCl}_3)\delta$ : 8.84 (1H, br s), 7.90-7.81 (3H, m), 7.66-7.58 (1H, m), 7.51-7.42 (2H, m), 7.38 (1H, d,  $J=1.3$  Hz), 7.15 (1H, dd,  $J=2.0$ , 8.7 Hz), 4.30-4.06 (4H, m), 1.70 (3H, s), 1.30-1.58 (6H, m).

STEP 5. Diethyl (2-benzoyl-6-chloro-1H-indol-3-yl)malonate

A mixture of diethyl  $\alpha$ -acetoxy-(2-benzoyl-6-chloro-1H-indol-3-yl)malonate (step 4, 5.0 g, 11 mmol), trifluoroacetic acid (3.3 ml, 44 mmol) and triethylsilane (2.1 ml, 13 mmol) in dichloromethane (80 ml) was heated at reflux temperature for 12 h 5 and then cooled and concentrated. The resulting residue was partitioned between saturated sodium bicarbonate (50 ml) and dichloromethane (80 ml). The aqueous layer was separated and extracted with dichloromethane (80 ml). The combined organic extracts were dried ( $MgSO_4$ ) and solvent removed. Crude product was purified by flush column chromatography eluting with ethyl acetate/hexane (1:4) to 10 afford 4.0 g (87 %) of the title compound as white solids.

$^1H$ -NMR ( $CDCl_3$ )  $\delta$ : 8.93 (1H, br s), 7.81-7.70 (3H, m), 7.68-7.60 (1H, m), 7.55-7.48 (2H, m), 7.32 (1H, s), 7.12 (1H, dd,  $J=1.8, 8.8$  Hz), 5.29 (1H, s), 4.26-4.09 (4H, m), 1.21 (6H, t,  $J=7.1$  Hz).

STEP 6. (2-Benzoyl-6-chloro-1H-indol-3-yl)acetic acid

15 Diethyl (2-benzoyl-6-chloro-1H-indol-3-yl)malonate (step 5, 4.4 g, 11 mmol) in a mixture of ethanol (120 ml) and 2N aqueous NaOH (15 ml) was heated at reflux temperature for 1 h. The mixture was cooled and concentrated, and the residue carefully acidified with 2N aqueous HCl (30 ml). The mixture was extracted with diethyl ether (150 ml x 3), and the combined extracts were dried ( $MgSO_4$ ) and 20 concentrated. The residual solids were recrystallized from ethyl acetate/hexane to afford 1.1 g (30%) of the title compound as pale yellow solids.

m.p.: 183-186 °C.

IR (KBr)  $\nu$ : 1700, 1610, 1520, 1425, 1330, 1000  $cm^{-1}$ .

18  $^1H$ -NMR ( $DMSO-d_6$ )  $\delta$ : 12.26 (1H, br s), 11.76 (1H, s), 7.77-7.66 (4H, m), 7.62-7.54 (2H, m), 7.48 (1H, d,  $J=1.8$  Hz), 7.13 (1H, dd,  $J=1.8, 8.7$  Hz), 3.80 (2H, s).

EXAMPLE 3(2-BENZOYL-6-CHLORO-1H-INDOL-3-YL)ACETIC ACID, SODIUM SALT

(2-Benzoyl-6-chloro-1H-indol-3-yl)acetic acid (Example 2, 480 mg, 1.5 mmol) in ethanol (10 ml) was treated with 2N aqueous NaOH (0.7 ml, 1.4 mmol) at room 30 temperature for 30 min. and then concentrated. The residue was dissolved in water

(10 ml) and washed with diethyl ether (15 ml x 2). The aqueous layer was concentrated to afford 350 mg (68%) of the title compound as pale brown solids.  
m.p.: 185-189 °C.

IR (KBr)  $\nu$ : 1523, 1380, 1230, 1060, 1004, 918  $\text{cm}^{-1}$ .

5  $^1\text{H-NMR}$  (DMSO-d<sub>6</sub>)  $\delta$ : 11.46 (1H, br s), 7.88-7.84 (2H, m), 7.66 (1H, d, J=8.4 Hz), 7.64-7.46 (3H, m), 7.39 (1H, d, J=1.8 Hz), 7.00 (1H, dd, J=1.8, 8.4 Hz), 3.32 (2H, s).

**EXAMPLE 4**

**[6-CHLORO-2-(2-METHYLBENZOYL)-1H-INDOL-3-YL]ACETIC ACID**

**STEP 1. 6-Chloro-2-(2-methylbenzoyl)-1-(phenylsulfonyl)indole**

10 The title compound was prepared according to the procedure described in step 2 of Example 2 (Method B) from 6-chloro-1-(phenylsulfonyl)indole (step 1 of Example 2, Method B) and *o*-toluoyl chloride.

tlc: R<sub>f</sub>=0.3 (ethyl acetate/hexane=1:10).

**STEP 2. 6-Chloro-2-(2-methylbenzoyl)indole**

15 The title compound was prepared according to the procedure described in step 3 of Example 2 (Method B) from 6-chloro-2-(2-methylbenzoyl)-1-(phenylsulfonyl)indole (step 1 ).

$^1\text{H-NMR}$  (CDCl<sub>3</sub>)  $\delta$ : 9.37 (1H, br s), 7.58 (2H, d, J=8.91Hz), 7.48 (1H, s), 7.42 (1H, d, J=1.49, 7.75Hz), 7.34-7.27 (2H, m), 7.12(2H, dd, J=1.81, 8.56Hz), 2.44 (3H, s)

20 **STEP 3. Diethyl  $\alpha$ -acetoxy-[6-chloro-2-(2-methylbenzoyl)-1H-indol-3-yl]malonate**

The title compound was prepared according to the procedure described in step 4 of Example 2 (Method B) from 6-chloro-2-(2-methylbenzoyl)indole (step 2).

$^1\text{H-NMR}$  (CDCl<sub>3</sub>)  $\delta$ : 8.52 (1H, br s), 7.78 (1H, d, J=8.88Hz), 7.48-7.13 (6H, m), 4.31, 4.16 (4H, m), 2.52 (3H, s), 1.96 (3H, s), 1.22 (6H, t, 7.26Hz).

25 **STEP 4. Diethyl [6-chloro-2-(2-methylbenzoyl)-1H-indol-3-yl]malonate**

The title compound was prepared according to the procedure described in step 5 of Example 2 (Method B) from diethyl  $\alpha$ -acetoxy-[6-chloro-2-(2-methylbenzoyl)-1H-indol-3-yl]malonate (step 3).

30  $^1\text{H-NMR}$  (CDCl<sub>3</sub>)  $\delta$ : 9.0 (1H, br s), 7.73 (1H, d, J=8.88Hz), 7.73-7.09 (5H, m), 7.11 (1H, dd, J=1.97, 8.75Hz), 4.89 (1H, s), 4.20-4.08 (4H, m), 2.35 (3H, s), 1.19 (6H, t,

J=7.1Hz).

STEP 5. [6-Chloro-2-(2-methylbenzoyl)-1H-indol-3-yl]acetic acid

The title compound was prepared according to the procedure described in step 6 of Example 2 (Method B) from diethyl [6-chloro-2-(2-methylbenzoyl)-1H-indol-3-yl]malonate (step 4).

m.p.: 150-152 °C.

IR (KBr) v: 3321, 1717, 1624, 1602, 1568, 1531, 1431, 1319, 1249, 1230 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.70 (1H, s), 7.69 (2H, d, J=8.72Hz), 7.51-7.31 (3H, m), 7.10 (2H, dd, J=1.97, 8.56Hz), 3.57 (2H, s), 2.24 (3H, s).

10 **EXAMPLE 5**

[6-CHLORO-2-(3-METHYLBENZOYL)-1H-INDOL-3-YL]ACETIC ACID

STEP 1. 6-Chloro-2-(3-methylbenzoyl)-1-(phenylsulfonyl)indole

The title compound was prepared according to the procedure described in step 2 of Example 2 (Method B) from 6-chloro-1-(phenylsulfonyl)indole (step 1 of Example 2, Method B) and *m*-toluoyl chloride.

tlc: R<sub>f</sub>=0.3 (ethyl acetate/hexane=1:10).

STEP 2. 6-Chloro-2-(3-methylbenzoyl)indole

The title compound was prepared according to the procedure described in step 3 of Example 2 (Method B) from 6-chloro-2-(3-methylbenzoyl)-1-(phenylsulfonyl)indole (step 1).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.37 (1H, s), 7.77 (2H, br s), 7.64 (1H, d, J=8.56Hz), 7.47-7.12 (5H, m), 2.47 (3H, s).

STEP 3. Diethyl α-acetoxy-[6-chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]malonate

The title compound was prepared according to the procedure described in step 4 of Example 2 (Method B) from 6-chloro-2-(3-methylbenzoyl)indole (step 2).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.80 (1H, br s), 7.83 (1H, d, J=8.88Hz), 7.67-7.32 (5H, m), 7.16 (1H, dd, J=1.81, 8.88Hz), 4.27-4.15 (4H, m), 2.39 (3H, s), 1.72 (3H, s), 1.29 (6H, t, J=7.26Hz).

STEP 4. Diethyl [6-chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]malonate

30 The title compound was prepared according to the procedure described in step 5 of Example 2 (Method B) from diethyl α-acetoxy-[6-chloro-2-(3-methylbenzoyl)-1H-

indol-3-yl]malonate (step 3).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.21 (1H, br s), 7.71 (1H, d, J=8.51Hz), 7.59-7.28 (5H, m), 7.10 (1H, dd, J=1.97, 8.72Hz), 5.27 (1H, s), 4.23-4.07 (4H, m), 2.40 (3H, s), 1.21 (6H, t, J=7.1Hz).

5 STEP 5. [6-Chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid

The title compound was prepared according to the procedure described in step 6 of Example 2 (Method B) from diethyl [6-chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]malonate (step 4).

m.p.: 182-184 °C.

10 IR (KBr) ν: 3313, 1699, 1616, 1568, 1533, 1408, 1325, 1265, 1203 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.75 (1H, s), 7.70(1H, d,J=8.75), 7.55-7.46 (5H, m), 7.12 (1H, dd, J=1.97, 8.72Hz), 3.75 (2H, s), 2.39 (3H, s).

EXAMPLE 6

[6-CHLORO-2-(4-METHYL BENZOYL)-1H-INDOL-3-YL]ACETIC ACID

15 STEP 1. 6-Chloro-2-(4-methylbenzoyl)-1-(phenylsulfonyl)indole

The title compound was prepared according to the procedure described in step 1 of Example 2 (Method B) from 6-chloro-1-(phenylsulfonyl)indole (step 1 of Example 2, Method B) and *p*-toluoyl chloride.

tlc: R<sub>f</sub>=0.3 (ethyl acetate/hexane=1:10).

20 STEP 2. 6-Chloro-2-(4-methylbenzoyl)indole

The title compound was prepared according to the procedure described in step 2 of Example 2 (Method B) from 6-chloro-2-(4-methylbenzoyl)-1-(phenylsulfonyl)indole (step 1).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.37 (1H, br s), 7.90 (2H, d, J=8.6Hz), 7.63 (1H, d, J=8.9Hz).

25 7.48 (1H, s), 7.34 (2H, d, J=8.6Hz), 7.16-7.10 (2H, m), 2.47 (3H, s).

STEP 3. Diethyl α-acetoxy-[6-chloro-2-(4-methylbenzoyl)-1H-indol-3-yl]malonate

The title compound was prepared according to the procedure described in step 4 of Example 2 (Method B) from 6-chloro-2-(4-methylbenzoyl)indole (step 2).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.65 (1H, br s), 7.84 (1H, d, J=8.9Hz), 7.76 (2H, d, J=8.2Hz).

30 7.39-7.37 (1H, m), 7.27 (2H, d, J=8.2Hz), 7.16 (1H, dd, J=1.8, 8.2Hz), 4.36-4.16 (4H,

m), 2.44 (3H, s), 1.72 (3H, s), 1.34-1.22 (6H, m).

STEP 4. Diethyl [6-chloro-2-(4-methylbenzoyl)-1H-indol-3-yl]malonate

The title compound was prepared according to the procedure described in step 5 of Example 2 (Method B) from diethyl  $\alpha$ -acetoxy-[6-chloro-2-(4-methylbenzoyl)-1H-indol-3-yl]malonate (step 3).

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.83 (1H, br s), 7.76 (1H, d,  $J=8.7\text{Hz}$ ), 7.71 (2H, d,  $J=8.2\text{Hz}$ ), 7.39-7.36 (1H, m), 7.32 (2H, d,  $J=8.2\text{Hz}$ ), 7.14 (1H, dd,  $J=2.0, 8.7\text{Hz}$ ), 5.30 (1H, s), 4.26-4.14 (4H, m), 2.47 (3H, s), 1.22 (6H, t,  $J=7.1\text{Hz}$ ).

STEP 5. [6-Chloro-2-(4-methylbenzoyl)-1H-indol-3-yl]acetic acid

10 The title compound was prepared according to the procedure described in step 6 of Example 2 (Method B) from diethyl [6-chloro-2-(4-methylbenzoyl)-1H-indol-3-yl]malonate (step 4).

m.p.: 182-184 °C.

IR (KBr)  $\nu$ : 3321, 1705, 1616, 1602, 1566, 1529, 1431, 1323, 1257, 1230  $\text{cm}^{-1}$ .

15  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$ : 11.72 (1H, s), 7.74-7.64 (3H, m), 7.49-7.45 (1H, m), 7.39 (2H, d,  $J=8.1\text{Hz}$ ), 7.16-7.09 (1H, m), 3.81 (2H, s), 2.43 (3H, s).

EXAMPLE 7

[6-CHLORO-2-(3-CHLOROBENZOYL)-1H-INDOL-3-YL]ACETIC ACID

STEP 1. 6-Chloro-2-[(N-methoxy-N-methylamino)carbonyl]indole

20 To a stirred suspension of 6-chloroindole-2-carboxylic acid (H.N.Rydon and J.C.Tweddle, *J.Chem.Soc.*, 1955, 3499., 7.0g, 36 mmol) in thionyl chloride (30 ml) was added dropwise DMF (1 ml). After stirring for 30 min., the mixture was concentrated, and the residue was dissolved in dichloromethane (100 ml) and cooled to 0 °C. To the mixture was added *N,O*-dimethylhydroxylamine hydrochloride (7.0 g, 72 mmol) and pyridine (15 ml). After stirring 2h, the mixture was quenched with water (100 ml), and extracted with dichloromethane (150 ml x 2). The combined organic extracts were washed with 2N aqueous HCl (100 ml), saturated sodium bicarbonate (100 ml), brine (100 ml), and dried ( $\text{MgSO}_4$ ). Removal of solvent afforded 8.2 g (96 %) of the title compound as yellow solids.

30  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 9.48 (1H, br s), 7.60 (1H, d,  $J=8.6\text{Hz}$ ), 7.46-7.41 (1H, m), 7.22-7.18 (1H, m), 7.11 (1H, dd,  $J=8.6, 1.8\text{Hz}$ ), 3.85 (3H, s), 3.44 (3H, s).

STEP 2. 6-Chloro-2-(3-chlorobenzoyl)indole

To a stirred solution of 6-chloro-2-[(N-methoxy-N-methylamino)carbonyl]indole (step 1, 610 mg, 2.56 mmol) and 3-bromochlorobenzene (1.47 g, 7.67 mmol) in THF (20 ml) at -78°C was added dropwise *n*-butyllithium 5 (1.54M in hexane, 4.90 ml, 7.67 mmol). After stirring for 1h, the mixture was quenched with saturated ammonium chloride (20 ml), and extracted with ethyl acetate (50 ml x 2). The combined organic extracts were washed with 2N aqueous HCl (50 ml), saturated sodium bicarbonate (50 ml), brine (50 ml), and dried ( $\text{MgSO}_4$ ). After removal of solvent, the crude product was purified by flash column chromatography 10 eluting with ethyl acetate/hexane (1:10) to afford 565 mg (76 %) of the title compound as pale brown solids.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 9.31 (1H, br s), 7.94 (1H, t,  $J=1.9\text{Hz}$ ), 7.85 (1H, dt,  $J=1.9, 7.6\text{Hz}$ ), 7.65 (1H, d,  $J=8.4\text{Hz}$ ), 7.63-7.58 (1H, m), 7.52-7.45 (2H, m), 7.18-7.12 (2H, m).

STEP 3. Diethyl  $\alpha$ -acetoxy-[6-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]malonate

15 The title compound was prepared according to the procedure described in step 4 of Example 2 (Method B) from 6-chloro-2-(3-chlorobenzoyl)indole (step 2).

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.88 (1H, br s), 7.87-7.74 (3H, m), 7.61-7.56 (1H, m), 7.43 (1H, d,  $J=7.6\text{Hz}$ ), 7.41-7.38 (1H, m), 7.20-7.14 (1H, m), 4.30-4.14 (4H, m), 1.74 (3H, s), 1.20 (6H, t,  $J=8.2\text{Hz}$ ).

20 STEP 4. Diethyl [6-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]malonate

The title compound was prepared according to the procedure described in step 5 of Example 2 (Method B) from diethyl  $\alpha$ -acetoxy-[6-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]malonate (step 3).

25  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.87 (1H, br s), 7.79-7.74 (2H, m), 7.70-7.58 (2H, m), 7.47 (1H, t,  $J=8.1\text{Hz}$ ), 7.39-7.37 (1H, m), 7.15 (1H, dd,  $J=1.8, 8.7\text{Hz}$ ), 5.19 (1H, s), 4.27-4.10 (4H, m), 1.22 (6H, t,  $J=7.1\text{Hz}$ ).

STEP 5. [6-Chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid

The title compound was prepared according to the procedure described in step 6 of Example 2 (Method B) from diethyl [6-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]malonate (step 4).

m.p.: 199-201 °C.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.25 (1H, br s), 11.81 (1H, s), 7.79-7.57 (5H, m), 7.48 (1H, d, J=1.8Hz), 7.14 (1H, dd, J=1.8, 8.7Hz), 3.81 (2H, s).

**EXAMPLE 8**

- 5    **METHYL [6-CHLORO-2-(4-CHLOROBENZOYL)-1H-INDOL-3-YL]ACETATE**

**Method A**

**STEP 1. Methyl trans 4-chloro-2-(phenylsulfonylamino)cinnamate**

To a solution of methyl *trans*-2-amino-4-chlorocinnamate (R.W.Carling et al., *J.Med.Chem.*, 1993, 36, 3397., 30.7 g, 0.15 mol) and pyridine (36 ml, 0.45 mol) in dichloromethane (500 ml) was added benzenesulfonyl chloride (20 ml, 0.16 mol). After stirring for 20 h, methanol (50 ml) was added and the mixture was concentrated. The residual solids were dissolved in dichloromethane (700 ml) and washed with 2N aqueous HCl (150 ml), brine (150 ml) and dried (MgSO<sub>4</sub>). After removal of solvent, the residual solids were recrystallized from ethanol to give 40 g (76 %) of the title compound as pale yellow solids.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.77-7.71 (2H, m), 7.59-7.52 (1H, m), 7.48-7.35 (5H, m), 7.20 (1H, dd, J=2.0, 8.4 Hz), 6.85 (1H, br s), 6.15 (1H, d, J=15.8 Hz), 3.78 (3H, s).

**STEP 2. methyl [6-chloro-2-(4-chlorobenzoyl)-1-(phenylsulfonyl)indolin-3-yl]acetate**

A mixture of methyl *trans*-4-chloro-2-(phenylsulfonylamino)cinnamate (step 1) 20 1.1 g, 3.1 mmol), 4-chlorophenacylbromide (1.1 g, 4.6 mmol) and potassium carbonate (2.1 g, 15.4 mmol) in acetone (10 ml) was stirred at room temperature for 1.5 h. The mixture was filtered and the filtrate concentrated. The residual solids were recrystallized from ethyl acetate/ hexane to afford 0.91 g (59%) of the title compound as pale yellow solids.

25    <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.97-7.94 (2H, m), 7.86-7.81 (2H, m), 7.65-7.58 (1H, m), 7.55-7.46 (5H, m), 7.02 (1H, dd, J=2.0, 8.2 Hz), 6.90 (1H, d, J=8.2 Hz), 5.99 (1H, d, J=9.7 Hz), 4.00-3.87 (1H, m), 3.41 (3H, s), 2.63 (1H, dd, J=6.3, 17.6 Hz), 2.51 (1H, dd, J=6.3, 17.6 Hz).

**STEP 3. Methyl [6-Chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetate**

30    To a stirred solution of methyl [6-chloro-2-(4-chlorobenzoyl)-1-(phenylsulfonyl)indolin-3-yl]acetate (step 2, 50 mg, 0.10 mmol) in THF was added 1,8-

diazabicyclo[5.4.0]undec-7-ene (DBU, 30  $\mu$ l, 0.20 mmol). After stirring for 15h, the mixture was quenched with water (30 ml), and extracted with ethyl acetate (50 ml). The extract was washed with 2N aqueous HCl (30 ml), saturated sodium bicarbonate (30 ml), brine (30 ml), and dried ( $MgSO_4$ ). Removal of solvent afforded 34 mg  
5 (93 %) of the title compound as yellow solids.

MS (EI) m/z : 361 ( $M^+$ ).

$^1H$ -NMR ( $CDCl_3$ )  $\delta$ : 8.90 (1H, br s), 7.74 (2H, d,  $J=8.6Hz$ ), 7.56 (1H, d,  $J=8.6Hz$ ),  
7.49 (2H, d,  $J=8.6Hz$ ), 7.36 (1H, d,  $J=1.6Hz$ ), 7.16 (1H, dd,  $J=1.6, 8.6Hz$ ), 3.81 (2H, s),  
3.66 (3H, s).

## 10 Method B

A mixture of methyl *trans*-4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of Method A, 0.70 g, 2.0 mmol), 4-chlorophenacyl bromide (0.51 g, 2.2 mmol), and potassium carbonate (0.83 g, 6.0 mmol) in acetone (20 ml) was stirred at room temperature. After stirring for 2h, cesium carbonate (2.0 g, 6.0 mmol) was added and  
15 the stirring was continued for an additional 4h. The mixture was concentrated and the residue was diluted in water (100 ml). The aqueous mixture was extracted with ethyl acetate (100 ml x 2). The combined organic extracts were washed with 2N aqueous HCl (100 ml), saturated sodium bicarbonate (100 ml), brine (100 ml), and dried ( $MgSO_4$ ). After removal of solvent, the solids were recrystallized from ethanol to  
20 afford 0.44 g (61 %) of the title compound.

MS and NMR spectra were identical with those of the compound prepared in step 3.

## EXAMPLE 9

### [6-CHLORO-2-(4-CHLOROBENZOYL)-1H-INDOL-3-YL]ACETIC ACID

#### **Method A**

##### 25 STEP 1. 6-Chloro-2-(4-chlorobenzoyl)indole

The title compound was prepared according to the procedure described in step 2 of Example 7 from 6-chloro-2-[(N-methoxy-N-methylamino)carbonyl]indole (Example 7, step 1) and 4-bromochlorobenzene.

$^1H$ -NMR ( $DMSO-d_6$ )  $\delta$ : 12.14 (1H, br s), 7.97 (2H, d,  $J=8.4Hz$ ), 7.76 (1H, d,  $J=8.6Hz$ ),  
30 7.66 (2H, d,  $J=8.4Hz$ ), 7.54-7.50 (1H, m), 7.20 (1H, s), 7.14 (1H, dd,  $J=2.0, 8.6Hz$ ).

##### STEP 2. Diethyl $\alpha$ -acetoxy-[6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]malonate

The title compound was prepared according to the procedure described in step 4 of Example 2 (Method B) from 6-chloro-2-(4-chlorobenzoyl)indole (step 1).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.83 (1H, br s), 7.87-7.77 (3H, m), 7.48-7.36 (3H, m), 7.17 (1H, dd, J=2.0, 8.9Hz), 4.28-4.14 (4H, m), 1.73 (3H, s), 1.20 (6H, t, J=7.1Hz).

5 **STEP 3. Diethyl [6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]malonate**

The title compound was prepared according to the procedure described in step 5 of Example 2 (Method B) from diethyl α-acetoxy-[6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]malonate (step 2).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.91 (1H, br s), 7.75 (2H, d, J=8.6Hz), 7.75-7.69 (1H, m), 7.50 (2H, d, J=8.6Hz), 7.29 (1H, d, J=1.8Hz), 7.13 (1H, dd, J=1.8, 8.7Hz), 5.23 (1H, s), 4.28-4.07 (4H, m), 1.23 (6H, t, J=7.2Hz).

**STEP 4. [ 6-Chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid**

The title compound was prepared according to the procedure described in step 6 of Example 2 (Method B) from diethyl [6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]malonate (step 3).

m.p.: 189-190 °C.

IR (KBr) v: 3309, 1699, 1616, 1525, 1431, 1325, 1255, 1226, 1091 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.78 (1H, s), 7.80-7.72 (3H, m), 7.65 (2H, d, J=8.6Hz), 7.47 (1H, d, J=1.8Hz), 7.13 (1H, dd, J=1.8, 8.7Hz), 3.83 (2H, s).

20 **Method B**

**[6-Chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid**

A mixture of methyl [6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetate (Example 8, 1.80 g) and 2N aqueous NaOH (7.5 ml) in MeOH-THF (10 ml-10 ml) was stirred at 80 °C for 1h. The mixture was cooled and concentrated. The residue was dissolved in water (150 ml) and washed with diethyl ether (50 ml). The aqueous layer was acidified with 2N aqueous HCl (10 ml), and extracted with ethyl acetate (100 ml x 2). The combined organic extracts were washed with brine (50 ml), dried (MgSO<sub>4</sub>), and concentrated. The residual solids were recrystallized from toluene to afford 1.58 g (91 %) of the title compound.

30 IR and NMR spectra were identical with those of the compound prepared by Method A.

**EXAMPLE 10****[6-CHLORO-2-(3-FLUOROBENZOYL)-1H-INDOL-3-YL]ACETIC ACID****STEP 1. 6-Chloro-2-(3-fluorobenzoyl)indole**

5 The title compound was prepared according to the procedure described in step 2 of Example 7 from 6-chloro-2-[(N-methoxy-N-methylamino)carbonyl]indole (Example 7, step 1) and 3-bromofluorobenzene.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.28 (1H, br s), 7.79-7.75 (1H, m), 7.68-7.63 (2H, m), 7.56-7.48 (2H, m), 7.36-7.30 (1H, m), 7.17-7.14 (2H, m).

**STEP 2. Diethyl α-acetoxy-[6-chloro-2-(3-fluorobenzoyl)-1H-indol-3-yl]malonate**

10 The title compound was prepared according to the procedure described in step 4 of Example 2 (Method B) from 6-chloro-2-(3-fluorobenzoyl)indole (step 1).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.15 (1H, br s), 8.83 (1H, d, J=8.72Hz), 7.66-7.27 (5H, m), 7.17 (1H, dd, J=2.00, 8.72Hz), 4.25-4.13 (4H, m), 1.75 (3H, s), 1.19 (6H, t, J=7.07Hz).

**STEP 3. Diethyl [6-chloro-2-(3-fluorobenzoyl)-1H-indol-3-yl]malonate**

15 The title compound was prepared according to the procedure described in step 5 of Example 2 (Mehod B) from diethyl α-acetoxy-[6-chloro-2-(3-fluorobenzoyl)-1H-indol-3-yl]malonate (step 2).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.91 (1H, br s), 7.77-7.12 (7H, m), 5.21 (1H, s), 4.25-4.11 (4H, m), 1.22 (6H, t, J=7.07Hz).

**STEP 4. [6-Chloro-2-(3-fluorobenzoyl)-1H-indol-3-yl]acetic acid**

The title compound was prepared according to the procedure described in step 6 of Example 2 (Method B) from diethyl [6-chloro-2-(3-fluorobenzoyl)-1H-indol-3-yl]malonate (step 3).

m.p.: 278-281 °C.

25 IR (KBr) v: 3385, 1697, 1638, 1583, 1541, 1508, 1420, 1400, 1315, 1261, 1236 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.79 (1H, s), 7.76-7.48 (7H, m), 7.13 (1H, dd, J=1.97, 8.56Hz), 3.80 (2H, s).

**EXAMPLE 11****[6-CHLORO-2-(4-FLUOROBENZOYL)-1H-INDOL-3-YL]ACETIC ACID****STEP 1. 6-Chloro-2-(4-fluorobenzoyl)indole**

The title compound was prepared according to the procedure described in step 2 of Example 7 from 6-chloro-2-[(N-methoxy-N-methylamino)carbonyl]indole (Example 7, step 1) and 4-bromofluorobenzene.

5       $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 9.29 (1H, br s), 8.05-8.00 (2H, m), 7.64 (1H, d,  $J=8.72\text{Hz}$ ), 7.48-  
7.11 (5H, m).

**STEP 2. Diethyl  $\alpha$ -acetoxy-[6-chloro-2-(4-fluorobenzoyl)-1H-indol-3-yl]malonate**

The title compound was prepared according to the procedure described in step 4 of Example 2 (Method B) from 6-chloro-2-(4-fluorobenzoyl)indole (step 1).

10      $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 9.20 (1H, br s), 7.92-7.11 (7H, m), 4.25-4.14 (4H, m), 1.73 (3H, s), 1.20 (6H, t,  $J=7.10\text{Hz}$ ).

**STEP 3. Diethyl [6-chloro-2-(4-fluorobenzoyl)-1H-indol-3-yl]malonate**

The title compound was prepared according to the procedure described in step 5 of Example 2 (Method B) from diethyl  $\alpha$ -acetoxy-[6-chloro-2-(4-fluorobenzoyl)-1H-indol-3-yl]malonate (step 2).

15      $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 9.01 (1H, br s), 7.87-7.69 (2H, m), 7.71 (2H, d,  $J=8.91\text{ Hz}$ ), 7.37-  
7.10 (4H, m), 5.25 (1H, s), 4.26-4.11 (4H, m), 1.22 (6H, t,  $J=7.07\text{Hz}$ ).

**STEP 4. [6-Chloro-2-(4-fluorobenzoyl)-1H-indol-3-yl]acetic acid**

The title compound was prepared according to the procedure described in step 6 of Example 2 (Method B) from diethyl [6-chloro-2-(4-fluorobenzoyl)-1H-indol-3-yl]malonate (step 3).

m.p.: 181-183 °C.

IR (KBr)  $\nu$ : 3309, 1701, 1616, 1601, 1566, 1527, 1508, 1419, 1323, 1257, 1229 cm<sup>-1</sup>.

17      $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$ : 11.75 (1H, s), 7.87-7.82 (2H, m), 7.73 (1H, d,  $J=8.72\text{ Hz}$ ), 7.47-  
7.36 (3H, m), 7.12 (1H, dd,  $J=1.84, 8.72\text{Hz}$ ), 3.78 (2H, s).

25     **EXAMPLE 12**

**[2-(3-BROMOBENZOYL)-6-CHLORO-1H-INDOL-3-YL]ACETIC ACID**

**STEP 1. 2-(3-Bromobenzoyl)-6-chloroindole**

The title compound was prepared according to the procedure described in step 2 of Example 7 from 6-chloro-2-[(N-methoxy-N-methylamino)carbonyl]indole (Example 7, step 1) and 3-bromoiodobenzene.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.28 (1H, br s), 8.11-8.08 (1H, m), 7.93-7.87 (1H, m), 7.79-7.73 (1H, m), 7.65 (1H, d, J=8.6Hz), 7.50-7.38 (2H, m), 7.19-7.01 (2H, m).

**STEP 2. Diethyl α-acetoxy-[2-(3-bromobenzoyl)-6-chloro-1H-indol-3-yl]malonate**

The title compound was prepared according to the procedure described in step 4  
5 of Example 2 (Method B) from 2-(3-bromobenzoyl)-6-chloroindole (step 1).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.73 (1H, br s), 7.93 (1H, t, J=1.8Hz), 7.85 (1H, d, J=8.6Hz),  
7.82-7.72 (2H, m), 7.42-7.32 (2H, m), 7.18 (1H, dd, J=2.0, 8.6Hz), 4.32-4.16 (4H, m),  
1.75 (3H, s), 1.20 (6H, t, J=7.1Hz).

**STEP 3. Diethyl [2-(3-bromobenzoyl)-6-chloro-1H-indol-3-yl]malonate**

10 The title compound was prepared according to the procedure described in step 5  
of Example 2 (Method B) from diethyl α-acetoxy-[2-(3-bromobenzoyl)-6-chloro-1H-  
indol-3-yl]malonate (step 2).

15 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.88 (1H, br s), 7.92-7.90 (1H, m), 7.80-7.68 (3H, m), 7.45-7.36  
(2H, m), 7.15 (1H, dd, J=1.8, 8.7Hz). 5.20 (1H, s), 4.30-4.10 (4H, m), 1.23 (6H, t,  
J=7.2Hz).

**STEP 4. [2-(3-Bromobenzoyl)-6-chloro-1H-indol-3-yl]acetic acid**

The title compound was prepared according to the procedure described in step 6  
of Example 2 (Method B) from diethyl [2-(3-bromobenzoyl)-6-chloro-1H-indol-3-  
yl]malonate (step 3).

20 m.p.: 215-218 °C.

IR (KBr) ν: 3369, 1710, 1604, 1558, 1533, 1423, 1319, 1253, 1228 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.81 (1H, s), 7.92-7.83 (2H, m), 7.78-7.70 (2H, m), 7.54 (1H,  
t, J=7.8Hz), 7.48 (1H, d, J=2.0Hz), 7.13 (1H, dd, J=2.0, 8.7Hz), 3.80 (2H, s).

**EXAMPLE 13**

25 **[2-(4-BROMOBENZOYL)-6-CHLORO-1H-INDOL-3-YL]ACETIC ACID**

**STEP 1. 2-(4-Bromobenzoyl)-6-chloroindole**

The title compound was prepared according to the procedure described in step 2  
of Example 7 from 6-chloro-2-[(N-methoxy-N-methylamino)carbonyl]indole (Example  
7, step 1) and 4-bromoiodobenzene.

30 <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.28 (1H, br s), 7.88 (2H, d, J=8.7Hz), 7.80 (2H, d, J=8.7Hz),

7.76 (1H, d, J=8.7Hz), 7.53-7.50 (1H, m), 7.22-7.19 (1H, m), 7.13 (1H, dd, J=2.0, 8.7Hz).

**STEP 2. Diethyl  $\alpha$ -acetoxy-[2-(4-bromobenzoyl)-6-chloro-1H-indol-3-yl]malonate**

The title compound was prepared according to the procedure described in step 4  
5 of Example 2 (Method B) from 2-(4-bromobenzoyl)-6-chloroindole (step 1).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.72 (1H, br s), 7.84 (1H, d, J=8.7Hz), 7.73 (2H, d, J=8.4Hz),  
7.62 (2H, d, J=8.4Hz), 7.38 (1H, d, J=1.8Hz), 7.18 (1H, dd, J=1.8, 8.7Hz), 4.28-4.14  
(4H, m), 1.73 (3H, s), 1.20 (6H, t, J=7.1Hz).

**STEP 3. Diethyl [2-(4-bromobenzoyl)-6-chloro-1H-indol-3-yl]malonate**

10 The title compound was prepared according to the procedure described in step 5  
of Example 2 (Method B) from diethyl  $\alpha$ -acetoxy-[2-(4-bromobenzoyl)-6-chloro-1H-  
indol-3-yl]malonate (step 2).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.86 (1H, br s), 7.75 (1H, d, J=8.4Hz), 7.67 (4H, s), 7.37-7.32  
(1H, m), 7.18-7.12 (1H, m), 5.22 (1H, s), 4.26-4.10 (4H, m), 1.23 (6H, t, J=7.1Hz).

15 **STEP 4.[2-(4-Bromobenzoyl)-6-chloro-1H-indol-3-yl]acetic acid**

The title compound was prepared according to the procedure described in step 6  
of Example 2 (Method B) from diethyl [2-(4-bromobenzoyl)-6-chloro-1H-indol-3-  
yl]malonate (step 3).

m.p.:199-201 °C.

20 IR (KBr) ν: 3300, 1699, 1618, 1587, 1525, 1433, 1406, 1325, 1255, 1226 cm<sup>-1</sup>

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.78 (1H, s), 7.80 (2H, d, J=8.4Hz), 7.75 (1H, d, J=8.6Hz),  
7.69 (2H, d, J=8.4Hz), 7.47 (1H, d, J=1.8Hz), 7.13 (1H, dd, J=1.8, 8.6Hz), 3.84 (2H, s)

**EXAMPLE 14**

**[6-CHLORO-2-(3-TRIFLUOROMETHYLBENZOYL)-1H-INDOL-3-YL]ACETIC**

25 **ACID**

**STEP 1. 6-Chloro-2-(3-trifluoromethylbenzoyl)indole**

The title compound was prepared according to the procedure described in step 2  
of Example 7 from 6-chloro-2-[(N-methoxy-N-methylamino)carbonyl]indole (Example  
7, step 1) and 3-bromobenzotrifluoride.

30 <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.23 (1H, br s), 8.28-8.04 (3H, m), 7.89-7.75 (2H, m), 7.55-

7.51 (1H, m), 7.22-7.12 (2H, m).

**STEP 2. Diethyl α-acetoxy-[6-chloro-2-(3-trifluoromethylbenzoyl)-1H-indol-3-yl]malonate**

The title compound was prepared according to the procedure described in step 4  
5 of Example 2 (Method B) from 6-chloro-2-(3-trifluoromethylbenzoyl)indole (step 1).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.82 (1H, br s), 8.25-7.80 (4H, m), 7.68-7.57 (1H, m), 7.43-7.41  
(1H, m), 7.22-7.16 (1H, m), 4.36-4.20 (4H, m), 1.67 (3H, s), 1.20 (6H, t, J=7.1Hz).

**STEP 3. Diethyl [6-chloro-2-(3-trifluoromethylbenzoyl)-1H-indol-3-yl]malonate**

The title compound was prepared according to the procedure described in step 5  
10 of Example 2 (Method B) from diethyl α-acetoxy-[6-chloro-2-(3-trifluoromethylbenzoyl)-1H-indol-3-yl]malonate (step 2).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.91 (1H, br s), 8.08-8.03 (1H, m), 8.02-7.87 (2H, m), 7.76 (1H, d,  
J=9.0Hz), 7.73-7.64 (1H, m), 7.39-7.36 (1H, m), 7.15 (1H, dd, J=1.8, 9.0Hz). 5.15 (1H,  
s), 4.26-4.10 (4H, m), 1.22 (6H, t, J=7.2Hz).

**STEP 4. [6-Chloro-2-(3-trifluoromethylbenzoyl)-1H-indol-3-yl]acetic acid**

The title compound was prepared according to the procedure described in step 6  
of Example 2 (Method B) from diethyl [6-chloro-2-(3-trifluoromethylbenzoyl)-1H-indol-3-yl]malonate (step 3).

m.p.: 194-196 °C.

20 IR (KBr) ν: 3371, 1705, 1631, 1421, 1307, 1228, 1168, 1122, 1072 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.86 (1H, s), 8.10-7.98 (3H, m), 7.83 (1H, t, J=7.7Hz), 7.75  
(1H, d, J=8.6Hz), 7.49 (1H, d, J=2.0Hz), 7.15 (1H, dd, J=2.0, 8.6Hz), 3.80 (2H, s).

**EXAMPLE 15**

**[6-CHLORO-2-(4-TRIFLUOROMETHYL BENZOYL)-1H-INDOL-3-YL]ACETIC**

**ACID**

**STEP 1. 6-Chloro-1-(phenylsulfonyl)-2-(4-trifluoromethylbenzoyl)indole**

The title compound was prepared according to the procedure described in step 2  
of Example 2 (Method B) from 6-chloro-1-(phenylsulfonyl)indole (step 1 of Example 2,  
Method B) and 4-trifluoromethylbenzoyl chloride.

30 tlc: R<sub>f</sub>=0.2 (ethyl acetate/hexane=1:4).

STEP 2. 6-Chloro-2-(4-trifluoromethylbenzoyl)indole

The title compound was prepared according to the procedure described in step 3 of Example 2 (Method B) from 6-chloro-1-phenylsulfonyl-2-(4-trifluoromethylbenzoyl) indole (step 1).

5     <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.53 (1H, br s), 7.94 (4H, dd, J=8.24, 69.1Hz), 7.63 (1H, d, J=8.56Hz), 7.49-7.11 (3H, m).

STEP 3. Diethyl α-acetoxy-[6-chloro-2-(4-trifluoromethylbenzoyl)-1H-indol-3-yl]malonate

10   The title compound was prepared according to the procedure described in step 4 of Example 2 (Method B) from 6-chloro-2-(4-trifluoromethylbenzoyl)indole (step 2).

1H-NMR (CDCl<sub>3</sub>) δ: 8.66 (1H, br s), 7.98 (2H, d, J=8.24Hz), 7.87 (1H, d, J=8.91Hz), 7.75 (2H, d, J=8.07Hz), 7.39 (1H, d, J=1.81Hz), 7.19 (1H, dd, J=1.81, 7.10Hz), 4.36-4.16 (4H, m), 1.70 (3H, s), 1.34-1.22 (6H, m).

STEP 4. Diethyl [6-chloro-2-(4-trifluoromethylbenzoyl)-1H-indol-3-yl]malonate

15   The title compound was prepared according to the procedure described in step 5 of Example 2 (Method B) from diethyl α-acetoxy-[6-chloro-2-(4-trifluoromethylbenzoyl)-1H-indol-3-yl]malonate (step 3).

1H-NMR (CDCl<sub>3</sub>) δ: 9.24 (1H, br s), 7.84 (4H, dd, J=7.91, 25.7Hz), 7.69-7.09 (3H, m), 5.24 (1H, s), 4.21-4.06 (4H, m), 1.21 (6H, t, J=7.07Hz).

20   STEP 5.[6-Chloro-2-(4-trifluoromethylbenzoyl)-1H-indol-3-yl]acetic acid

The title compound was prepared according to the procedure described in step 6 of Example 2 (Method B) from diethyl [6-chloro-2-(4-trifluoromethylbenzoyl)-1H-indol-3-yl]malonate (step 4).

25   <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.78 (1H, s), 7.94 (4H, s), 7.76 (1H, d, J=8.72Hz), 7.47 (1H, m), 7.14 (1H, d, J=1.81, 8.72), 3.81 (2H, s).

EXAMPLE 16[6-CHLORO-2-(3,4-DICHLOROBENZOYL)-1H-INDOL-3-YL]ACETIC ACIDSTEP 1. 6-Chloro-2-(3,4-dichlorobenzoyl)indole

The title compound was prepared according to the procedure described in step 2 of Example 7 from 6-chloro-2-[(N-methoxy-N-methylamino)carbonyl]indole (Example 7, step 1) and 1-bromo-3,4-dichlorobenzene.

tlc: R<sub>f</sub>=0.7 (ethyl acetate/hexane=1:3).

5 **STEP 2. Diethyl α-acetoxy-[6-chloro-2-(3,4-dichlorobenzoyl)-1H-indol-3-yl]malonate**

The title compound was prepared according to the procedure described in step 4 of Example 2 (Method B) from 6-chloro-2-(3,4-dichlorobenzoyl)indole (step 1).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.80 (1H, br s), 7.90-7.79 (2H, m), 7.71 (1H, dd, J=2.0, 8.4Hz), 7.57 (1H, d, J=8.4Hz), 7.40-7.35 (1H, m), 7.18 (1H, dd, J=1.8, 8.8Hz), 4.30-4.14 (4H, m), 1.77 (3H, s), 1.20 (6H, t, J=7.1Hz).

10 **STEP 3. Diethyl [6-chloro-2-(3,4-dichlorobenzoyl)-1H-indol-3-yl]malonate**

The title compound was prepared according to the procedure described in step 5 of Example 2 (Method B) from diethyl α-acetoxy-[6-chloro-2-(3,4-dichlorobenzoyl)-1H-indol-3-yl]malonate (step 2).

15 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.95 (1H, br s), 7.88 (1H, d, J=1.6Hz), 7.72 (1H, d, J=8.7Hz), 7.68-7.58 (2H, m), 7.28 (1H, d, J=1.6Hz), 7.14 (1H, dd, J=1.6, 8.7Hz). 5.18 (1H, s), 4.28-4.10 (4H, m), 1.23 (6H, t, J=7.1Hz).

**STEP 4. [6-Chloro-2-(3,4-dichlorobenzoyl)-1H-indol-3-yl]acetic acid**

The title compound was prepared according to the procedure described in step 6 of Example 2 (Method B) from diethyl [6-chloro-2-(3,4-dichlorobenzoyl)-1H-indol-3-yl]malonate (step 3).

m.p.: 206-209 °C.

IR (KBr) v: 3435, 1708, 1620, 1583, 1525, 1423, 1384, 1301, 1263, 1228 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.62 (1H, br s), 7.95-7.75 (3H, m), 7.68 (1H, d, J=8.7Hz), 7.42 (1H, d, J=2.0Hz), 7.02 (1H, dd, J=2.0, 8.7Hz), 3.50 (2H, s).

**EXAMPLE 17**

**(2-BENZOYL-4-CHLORO-1H-INDOL-3-YL)ACETIC ACID**

**STEP 1. 4-Chloro-2-[(N-methoxy-N-methylamino)carbonyl]indole**

The title compound was prepared according to the procedure described in step 1 of Example 7 employing 4-chloroindole-2-carboxylic acid (F. C. Uhle, *J. Amer. Chem. Soc.*, 1949, 71, 761).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.56 (1H, br s), 7.36-7.29 (2H, m), 7.24-7.12 (2H, m), 3.88 (3H, s), 3.45 (3H, s).

**STEP 2. 2-Benzoyl-4-chloroindole**

To a solution of 4-chloro-2-[(N-methoxy-N-methylamino)carbonyl]indole (step 5 1, 3.4 g, 0.014 mol) in THF (60 ml) cooled to -78 °C was added dropwise phenyllithium (1.8 M in cyclohexane/ether (7:3), 30 ml, 0.070 mol). After stirring for 1 h, the mixture was poured into water (80 ml) and extracted with ethyl acetate (80 ml x 2). After drying (MgSO<sub>4</sub>) and removal of solvent, the crude product was purified by flash column chromatography eluting with ethyl acetate/hexane (1:10) to afford 3.6 10 g (100 %) of the title compound as white solids.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.46 (1H, br s), 8.05-8.00 (2H, m), 7.73-7.51 (3H, m), 7.40 (1H, dd, J=1.0, 8.3 Hz), 7.33-7.24 (2H, m), 7.18 (1H, d, J=7.6 Hz).

**STEP 3. Diethyl α-acetoxy-(2-benzoyl-4-chloro-1H-indol-3-yl)malonate**

The title compound was prepared according to the procedure described in step 4 15 of Example 2 (Method B) from 2-benzoyl-4-chloroindole (step 2).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.49 (1H, br s), 7.98-7.92 (2H, m), 7.66-7.57 (1H, m), 7.53-7.43 (2H, m), 7.34 (1H, dd, J=2.0, 7.1 Hz), 7.21-7.15 (2H, m), 4.30-3.90 (4H, m), 2.08 (3H, s), 1.15 (6H, t, J=7.3 Hz).

**STEP 4. Diethyl (2-benzoyl-4-chloro-1H-indol-3-yl)malonate**

The title compound was prepared according to the procedure described in step 5 20 of Example 2 from diethyl α-acetoxy-(2-benzoyl-4-chloro-1H-indol-3-yl)malonate (step 3).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.88 (1H, br s), 7.83-7.77 (2H, m), 7.64-7.58 (1H, m), 7.55-7.46 (2H, m), 7.25-7.05 (3H, m), 5.86 (1H, s), 4.25-4.08 (4H, m), 1.23 (6H, t, J=7.3 Hz).

**STEP 5. (2-Benzoyl-4-chloro-1H-indol-3-yl)acetic acid**

The title compound was prepared according to the procedure described in step 6 of Example 2 (Method B) from diethyl (2-benzoyl-4-chloro-1H-indol-3-yl)malonate. m.p.: 206-209 °C (recrystallized from ethyl acetate/hexane).

IR (KBr) ν: 1700, 1575, 1245 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.20 (1H, br s), 11.98 (1H, s), 7.85-7.67 (3H, m), 7.63-7.55 (2H, m), 7.45 (1H, d, J=8.2 Hz), 7.25 (1H, t, J=8.2 Hz), 7.12 (1H, d, J=7.6 Hz), 4.02 (2H, s).

**EXAMPLE 18**

5 **[5-CHLORO-2-(3-METHYLBENZOYL)-1H-INDOL-3-YL]ACETIC ACID**

**STEP1. 5-Chloro-2-[(N-methoxy-N-methylamino)carbonyl]indole**

The title compound was prepared according to the procedure described in step 1 of Example 7 from 5-chloroindole-2-carboxylic acid.

10 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.68 (1H, br s), 7.68-7.65 (1H, m), 7.37 (1H, d, J=8.7 Hz), 7.23 (1H, d, J=1.6 Hz), 7.18-7.15 (1H, m), 3.85 (3H, s), 2.05 (3H, s).

**STEP2. 5-Chloro-2-(3-methylbenzoyl)indole**

The title compound was prepared according to the procedure described in step 2 of Example 17 from 5-chloro-2-[(N-methoxy-N-methylamino)carbonyl]indole (step 1) and 3-methylphenyllithium.

15 m.p.: 197.5-198 °C (recrystallized from ethyl acetate/hexane).

IR (KBr) v: 3310, 1626, 1603, 1583, 1516, 1406, 1377, 1337, 1269, 1178, 1134 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.39 (1H, br s), 7.28-7.76 (2H, m), 7.71-7.68 (1H, m), 7.46-7.38 (3H, m), 7.32 (1H, dd, J=8.7, 2.0 Hz), 7.08 (1H, dd, J=2.0, 0.8 Hz), 2.47 (3H, s).

**STEP3. Diethyl α-acetoxy-[5-chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]malonate**

20 The title compound was prepared according to the procedure described in step 4 of Example 2 (Method B) from 5-chloro-2-(3-methylbenzoyl)indole (step 2).

m.p.: 173-174 °C (recrystallized from ethyl acetate/hexane).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.64 (1H, br s), 7.91 (1H, br s), 7.69-7.61 (2H, m), 7.46-7.22 (4H, m), 4.30-4.16 (4H, m), 2.39 (3H, s), 1.72 (3H, s), 1.23 (3H, t, J=7.2 Hz).

25 **STEP4. Diethyl [5-chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]malonate**

The title compound was prepared according to the procedure described in step 5 of Example 2 (Method B) from diethyl α-acetoxy-[5-chloro-2-(3-methylbenzoyl)-1H-indol-3-yl] malonate (step 3).

m.p.: 143-144 °C (recrystallized from ethyl acetate/hexane).

30 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.88 (1H, br s), 7.84-7.80 (1H, m), 7.62-7.55 (2H, m), 7.48-7.36

(2H, m), 7.32-7.28 (2H, m), 5.27 (1H, s), 4.30-4.10 (4H, m), 2.42 (3H, s), 1.24 (3H, t, J=7.1 Hz).

**STEP5. [5-Chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid**

The title compound was prepared according to the procedure described in step 6  
5 of Example 2 (Method B) from diethyl [5-chloro-2-(3-methylbenzoyl)-1H-indol-3-  
yl]malonate.

m.p.: 241-242 °C (recrystallized from ethyl acetate/hexane).

IR (KBr) v: 3321, 1703, 1618, 1535, 1431, 1335, 1232, 1016, 808, 758 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.7 (1H, br s), 7.62 (1H, d, J=1.8 Hz), 7.45-7.30 (6H, m),

10 7.19 (1H, dd, J=8.6, 1.8 Hz), 3.63 (2H, s), 2.27 (3H, s).

**EXAMPLE 19**

**[5-CHLORO-2-(4-CHLOROBENZOYL)-1H-INDOL-3-YL]ACETIC ACID**

**STEP 1. 5-Chloro-2-(4-chlorobenzoyl)indole**

The title compound was prepared according to the procedure described in step 2  
15 of Example 7 from 5-chloro-2-[(N-methoxy-N-methylamino)carbonyl]indole (Example  
18, step 1) and 4-bromochlorobenzene.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.32 (1H, br s), 7.94 (2H, d, J=8.4Hz), 7.70 (1H, s), 7.53 (2H, d,  
J=8.4Hz), 7.42 (1H, d, J=8.9Hz), 7.34 (1H, dd, J=2.0, 8.9Hz), 7.07 (1H, s).

**STEP 2. Diethyl α-acetoxy-[5-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]malonate**

20 The title compound was prepared according to the procedure described in step 4  
of Example 2 (Method B) from 5-chloro-2-(4-chlorobenzoyl)indole (step 1).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.11 (1H, br s), 7.87 (1H, s), 7.76 (2H, d, J=8.6Hz), 7.41 (2H, d,  
J=8.6Hz), 7.27 (1H, d, J=8.7Hz), 7.22 (1H, dd, J=1.8, 8.7Hz), 4.25-4.14 (4H, m), 1.72  
(3H, s), 1.24-1.19 (6H, m).

25 **STEP 3. Diethyl [5-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]malonate**

The title compound was prepared according to the procedure described in step 5  
of Example 2 (Method B) from diethyl α-acetoxy-[5-chloro-2-(4-chlorobenzoyl)-1H-  
indol-3-yl]malonate (step 2).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.13 (1H, br s), 7.73 (2H, d, J=8.4Hz), 7.68 (1H, d, J=2.0Hz),

30 7.48 (2H, d, J=8.4Hz), 7.11 (1H, dd, J=2.0, 8.9Hz), 7.02 (1H, d, J=8.9Hz), 5.28 (1H, s).

4.24-4.03 (4H, m), 1.27-1.21 (6H, m).

**STEP 4. [5-Chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid**

The title compound was prepared according to the procedure described in step 6 of Example 2 (Method B) from diethyl [5-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]malonate (step 3).

m.p.: 220-224.°C (recrystallized from ethyl acetate/hexane).

IR (KBr) v: 3321, 1618, 1535, 1379, 1339, 1263, 1130, 1090, 1057, 1007 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.83 (1H, s), 7.80-7.75 (3H, m), 7.67-7.62 (2H, m), 7.48 (1H, d, J=8.7Hz), 7.31 (1H, dd, J=2.0, 8.7Hz), 3.84 (2H, s).

**10 EXAMPLE 20**

**[5-CHLORO-2-(3-CHLOROBENZOYL)-1H-INDOL-3-YL]ACETIC ACID**

**STEP 1. 5-Chloro-2-(3-chlorobenzoyl)indole**

The title compound was prepared according to the procedure described in step 2 of Example 7 from 5-chloro-2-[(N-methoxy-N-methylamino)carbonyl]indole (Example 18, step 1) and 3-bromochlorobenzene.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.28 (1H, br s), 7.95 (1H, t, J=1.7Hz), 7.88-7.84 (1H,m), 7.71 (1H, d, J=2.0Hz), 7.63-7.59 (1H, m), 7.49 (1H, t, J=7.7Hz), 7.42 (1H, d, J=8.7Hz), 7.34 (1H, dd, J=2.0, 8.7Hz), 7.10-7.09 (1H, m).

**STEP 2. Diethyl α-acetoxy-[5-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]malonate**

The title compound was prepared according to the procedure described in step 4 of Example 2 (Method B) from 5-chloro-2-(3-chlorobenzoyl)indole (step 1).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.94 (1H, br s), 7.91 (1H, d, J=1.8Hz), 7.79-7.76 (1H, m), 7.74 (1H, d, J=7.7Hz), 7.60-7.56 (1H, m), 7.42 (1H, t, J=7.7Hz), 7.33 (1H, d, J=8.7Hz), 7.27 (1H, dd, J=1.8, 8.7Hz), 4.37-4.19 (4H, m), 1.75 (3H, s), 1.26-1.20 (6H, m).

**25 STEP 3. Diethyl [5-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]malonate**

The title compound was prepared according to the procedure described in step 5 of Example 2 (Method B) from diethyl α-acetoxy-[5-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]malonate (step 2).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.04 (1H, br.s), 7.77-7.75 (2H, m), 7.68-7.58 (2H, m), 7.46 (1H, t,

30 J=7.7Hz), 7.24-7.20 (2H, m), 5.23 (1H, s), 4.27-4.14 (4H, m), 1.27-1.22 (6H, m).

STEP 4. [ 5-Chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid

The title compound was prepared according to the procedure described in step 6 of Example 2 (Method B) from diethyl [5-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]malonate (step 3).

5 m.p.: 243-247 °C (recrystallized from ethyl acetate/hexane).

IR (KBr)  $\nu$ : 3329, 1707, 1618, 1535, 1431, 1406, 1375, 1333, 1279, 1232, 1053 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 11.87 (1H, s), 7.81-7.68 (4H, m), 7.64-7.58 (1H, m), 7.49 (1H, d, J=8.9Hz), 7.32 (1H, dd, J=2.0, 8.9Hz), 3.82 (2H, s).

EXAMPLE 21

10 [2-(4-CHLOROBENZOYL)-5-FLUORO-1H-INDOL-3-YL]ACETIC ACID

STEP 1. 5-fluoro-2-[(N-methoxy-N-methylamino)carbonyl]indole

The title compound was prepared according to the procedure described in step 1 of Example 7 from 5-fluoroindole-2-carboxylic acid.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 10.15 (1H, br s), 7.41-7.36 (1H, m), 7.32 (1H, dd, J=2.5, 9.1Hz).

15 7.20-7.19 (1H, m), 7.09-7.01 (1H, m), 3.84 (3H, s), 3.47 (3H, s).

STEP 2. 2-(4-Chlorobenzoyl)-5-fluoro-indole

The title compound was prepared according to the procedure described in step 2 of Example 7 from 5-fluoro-2-[(N-methoxy-N-methylamino)carbonyl]indole (step 1) and 4-bromochlorobenzene.

20 <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 9.27 (1H, br s), 7.94 (2H, d, J=8.4Hz), 7.52 (2H, d, J=8.4Hz), 7.45-7.40 (1H, m), 7.37-7.33 (1H, m), 7.21-7.12 (1H, m), 7.10-7.09 (1H, m).

STEP 3. Diethyl  $\alpha$ -acetoxy-[2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]malonate

The title compound was prepared according to the procedure described in step 4 of Example 2 (Method B) from 2-(4-chlorobenzoyl)-5-fluoroindole (step 2).

25 <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 9.01 (1H, br s), 7.80-7.77 (2H, m), 7.58-7.54 (1H,m), 7.45-7.41 (2H, m), 7.36-7.27 (1H, m), 7.12-7.01 (1H, m), 4.29-4.15 (4H, m), 1.74 (3H, s), 1.28-1.17 (6H, m).

STEP 4. Diethyl [2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]malonate

The title compound was prepared according to the procedure described in step 5 of Example 2 (Method B) from diethyl  $\alpha$ -acetoxy-[2-(4-chlorobenzoyl)-5-fluoro-1H-

indol-3-yl]malonate (step 3).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.98 (1H, br s), 7.77-7.72 (2H, m), 7.51-7.46 (2H, m), 7.40 (1H, dd, J= 2.5, 9.7Hz), 7.18-7.13 (1H, m), 7.04-6.96 (1H, m), 5.28 (1H, s), 4.26-4.07 (4H, m), 1.30-1.18 (6H, m).

5 **STEP 5. [2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid**

The title compound was prepared according to the procedure described in step 6 of Example 2 (Method B) from diethyl [2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]malonate (step 4).

m.p.: 233-238 °C (recrystallized from ethyl acetate/hexane).

10 IR (KBr) v: 3317, 1707, 1624, 1609, 1587, 1526, 1458, 1408, 1344, 1263, 1242 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.73 (1H, s), 7.77 (2H, d, J=8.6Hz), 7.65 (2H, d, J=8.6Hz), 7.52-7.44 (2H, m), 7.22-7.15 (1H, m), 3.84 (2H, s).

**EXAMPLE 22**

**[2-(3-CHLOROBENZOYL)-5-FLUORO-1H-INDOL-3-YL]ACETIC ACID**

15 **STEP 1. 2-(3-chlorobenzoyl)-5-fluoroindole**

The title compound was prepared according to the procedure described in step 2 of Example 7 from 5-fluoro-2-[(N-methoxy-N-methylamino)carbonyl]indole (Example 21, step 1) and 3-bromochlorobenzene.

16 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.29 (1H, m), 7.96-7.94 (1H, m), 7.88-7.84 (1H, m), 7.63-7.59 (1H, m), 7.48 (1H, t, J=8.0Hz), 7.45-7.40 (1H, m), 7.36 (1H, dd, J=2.6, 8.6Hz), 7.20-7.11 (2H, m).

**STEP 2. Diethyl α-acetoxy-[2-(3-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]malonate**

The title compound was prepared according to the procedure described in step 4 of Example 2 (Method B) from 2-(3-chlorobenzoyl)-5-fluoroindole (step 1).

17 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.73 (1H, br s), 7.79-7.74 (2H, m), 7.61-7.56 (2H, m), 7.43 (1H, t, J=7.6Hz), 7.37-7.32 (1H, m), 7.13-7.06 (1H, m), 4.34-4.20 (4H, m), 1.76 (3H, s), 1.33-1.20 (6H, m).

**STEP 3. Diethyl [2-(3-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]malonate**

The title compound was prepared according to the procedure described in step 5 of Example 2 (Method B) from diethyl α-acetoxy-[2-(3-chlorobenzoyl)-5-fluoro-1H-

indol-3-yl]malonate (step 2).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.05 (1H, br s), 7.76-7.75 (1H, m), 7.68-7.64 (1H, m), 7.61-7.56 (1H, m), 7.48-7.40 (2H, m), 7.24-7.19 (1H, m), 7.08-7.00 (1H, m), 5.25 (1H, s), 4.28-4.07 (4H, m), 1.33-1.21 (6H, m).

5 **STEP 4. [ 2-(3-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid**

The title compound was prepared according to the procedure described in step 6 of Example 2 (Method B) from diethyl [2-(3-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]malonate (step 3).

m.p.: 208-212 °C (recrystallized from ethyl acetate/hexane).

10 IR (KBr) ν: 3337, 1709, 1618, 1560, 1529, 1477, 1458, 1427, 1408, 1335, 1304 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.78 (1H, s), 7.77-7.58 (4H, m), 7.52-7.46 (2H, m), 7.24-7.16 (1H, m), 3.82 (2H, s).

**EXAMPLE 23**

**[5-METHOXY-2-(3-METHYLBENZOYL)-1H-INDOL-3-YL]ACETIC ACID**

15 **STEP 1. 5-methoxy-2-[(N-methoxy-N-methylamino)carbonyl]indole**

The title compound was prepared according to the procedure described in step 1 of Example 7 from 5-methoxyindole-2-carboxylic acid.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.29 - 9.13 (1H, br), 7.33 (1H, d, J=8.9Hz), 7.19 - 7.14 (1H, m), 7.10 (1H, d, J=2.3Hz), 6.98 (1H, dd, J=8.9, 2.3Hz), 3.86 (3H, s), 3.84 (3H, s), 3.42 (3H, s).

20

**STEP 2. 5-Methoxy-2-(3-methylbenzoyl)indole**

The title compound was prepared according to the procedure described in step 2 of Example 17 from 5-methoxy-2-[(N-methoxy-N-methylamino)carbonyl]indole (step 1) and 3-methylphenyllithium.

25 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.65 - 9.45 (1H, br), 7.84 - 7.75 (2H, m), 7.46 - 7.35 (3H, m), 7.12 - 7.01 (3H, m), 3.85 (3H, s), 2.46 (3H, s).

**STEP 3. Diethyl α-acetoxy-[5-methoxy-2-(3-methylbenzoyl)-1H-indol-3-yl]malonate**

The title compound was prepared according to the procedure described in step 4 of Example 2 (Method B) from 5-methoxy-2-(3-methylbenzoyl)indole (step 2).

30 tlc: R<sub>f</sub>=0.45 (ethyl acetate/hexane=1:3).

STEP 4. Diethyl [5-methoxy-2-(3-methylbenzoyl)-1H-indol-3-yl]malonate

The title compound was prepared according to the procedure described in step 5 of Example 2 (Method B) from diethyl  $\alpha$ -acetoxy-[5-methoxy-2-(3-methylbenzoyl)-1H-indol-3-yl]malonate (step 3).

- 5    $^1\text{H-NMR}(\text{CDCl}_3)\delta$ : 9.52 - 9.13 (0.5H, m), 8.81 - 8.71 (0.5H, m), 7.80 - 7.72 (1H, m), 7.63 - 7.55 (1H, m), 7.47 - 7.00 (5H, m), 5.41(0.5H, s), 5.37 (0.5H, s), 4.27 - 4.15 (4H, m), 3.89 (1.5H, s), 3.84 (1.5H, s), 2.45 (1.5H, s), 2.43 (1.5H, s), 1.29 - 1.19 (6H, m).

STEP 5. [5-Methoxy-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid

- 10   The title compound was prepared according to the procedure described in step 6 of Example 2 (Method B) from diethyl [5-methoxy-2-(3-methylbenzoyl)-1H-indol-3-yl]malonate (step 4).

m.p.:230.4-232.0 °C (decomposed) (recyrstallized from ethyl acetate).

IR (KBr)  $\nu$ : 3310, 1705, 1614, 1583  $\text{cm}^{-1}$ .

- 15    $^1\text{H-NMR} (\text{DMSO-d}_6) \delta$ : 11.47 (1H, br s), 7.60-7.34 (5H, m), 7.16-7.09 (1H, m), 6.98 (1H, dd, J=9.0, 2.4Hz), 3.78 (5H, s), 2.40 (3H, s).

$^{13}\text{C-NMR} (\text{DMSO-d}_6) \delta$ : 188.1, 172.1, 153.8, 138.9, 137.9, 132.7, 132.3, 132.0, 129.2, 128.5, 128.0, 125.8, 117.0, 115.6, 113.6, 100.7, 55.3, 30.6, 20.8.

EXAMPLE 24(2-BENZOYL-7-CHLORO-1H-INDOL-3-YL)ACETIC ACID

- 20   STEP 1. 7-Chloro-2-[(N-methoxy-N-methylamino)carbonyl]indole

The title compound was prepared according to the procedure described in step 1 of Example 7 from 7-chloroindole-2-carboxylic acid (H. N. Rydon and J. C. Tweddle, *J. Chem. Soc.*, 1955, 3499).

- 25    $^1\text{H-NMR} (\text{CDCl}_3) \delta$ : 9.40 (1H, br s), 7.59 (1H, d, J=8.1 Hz), 7.32-7.25 (2H, m), 7.08 (1H, t, J=8.1 Hz), 3.85 (3H, s), 3.43 (3H, s).

STEP 2. 2-Benzoyl-7-chloroindole

The title compound was prepared according to the procedure described in step 2 of Example 17 from 7-chloro-2-[(N-methoxy-N-methylamino)carbonyl]indole (step 1) and phenyllithium.

- 30    $^1\text{H-NMR} (\text{CDCl}_3) \delta$ : 9.40 (1H, br s), 8.01-7.96 (2H, m), 7.70-7.50 (4H, m), 7.38 (1H, d, J=7.6 Hz), 7.18 (1H, d, J=2.0 Hz), 7.11 (1H, t, J=7.6 Hz).

STEP 3. Diethyl  $\alpha$ -acetoxy-(2-benzoyl-7-chloro-1H-indol-3-yl)malonate

The title compound was prepared according to the procedure described in step 4 of Example 2 (Method B) from 2-benzoyl-7-chloroindole (step 2).

- <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.76 (1H, br s), 7.92-7.81 (3H, m), 7.68-7.60 (1H, m), 7.53-7.45 (2H, m), 7.33 (1H, d, J=7.6 Hz), 7.15 (1H, t, J=8.2 Hz), 4.60-4.20 (4H, m), 1.71 (3H, s), 1.98 (6H, t, J=7.1 Hz).

STEP 4. Diethyl (2-benzoyl-7-chloro-1H-indol-3-yl)malonate

- The title compound was prepared according to the procedure described in step 5 of Example 2 (Method B) from diethyl  $\alpha$ -acetoxy-(2-benzoyl-7-chloro-1H-indol-3-yl)malonate (step 3).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.94 (1H, br s), 7.86-7.80 (2H, m), 7.75 (1H, d, J=8.1 Hz), 7.70-7.62 (1H, m), 7.55-7.50 (2H, m), 7.36 (1H, d, J=7.6 Hz), 7.13 (1H, t, J=7.6 Hz), 5.29 (1H, s), 4.25-4.11 (4H, m), 1.22 (6H, t, J=7.3 Hz).

STEP 5. (2-Benzoyl-7-chloro-1H-indol-3-yl)acetic acid

- The title compound was prepared according to the procedure described in step 6 of Example 2 (Method B) from diethyl (2-benzoyl-7-chloro-1H-indol-3-yl)malonate (step 4).

m.p.: 190-193 °C (recrystallized from ethyl acetate/hexane)

IR (KBr) ν: 1691, 1627, 1598, 1323, 1260 1199, 1010 cm<sup>-1</sup>.

- <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.90 (1H, br s), 7.82 (2H, m), 7.74-7.65 (2H, m), 7.62-7.58 (2H, m), 7.40 (1H, d, J=7.6 Hz), 7.13 (1H, t, J=7.6 Hz), 3.75 (2H, s).

EXAMPLE 25(2-BENZOYL-4,5-DICHLORO-1H-INDOL-3-YL)ACETIC ACIDSTEP 1. 4,5-dichloroindolyl-2-carboxylic acid

- To a suspension of ethyl 4,5-dichloroindole-2-carboxylate (Ishii et al., *Chem Pharm. Bull.*, 1974, 22, 1981, 1.8 g, 7.0 mmol) in ethanol (40 ml) was added 2N aqueous NaOH (10 ml) and the mixture was heated at reflux temperature for 2 h. The mixture was cooled to room temperature and concentrated. The residual solid was acidified with 2N aqueous HCl (30 ml) and extracted with diethyl ether (80 ml x 2). The organic extracts were dried (MgSO<sub>4</sub>) and concentrated to give 1.5 g (94 %) of the

title compound as yellow solids.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.34 (1H, br s), 7.47-7.39 (2H, m), 7.08 (1H, d, J=1.8 Hz).

**STEP 2. 4,5-Dichloro-2-[N-methoxy-N-methylamino)carbonyl]indole**

The title compound was prepared according to the procedure described in step 1  
5 of Example 7 from 4,5-dichloroindole-2-carboxylic acid (step 1).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.62 (1H, br s), 7.40-7.05 (3H, m), 3.88 (3H, s), 3.45 (3H, s).

**STEP 3. 2-Benzoyl-4,5-dichloroindole**

The titled compound was prepared according to the procedure described in step  
2 of Example 17 from 4,5-dichloro-2-[N-methoxy-N-methylamino)carbonyl]indole  
10 (step 2) and phenyllithium.

m.p.: 206-210 °C (recrysallized from ethyl acetate/hexane).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.58 (1H, br s), 8.05-7.98 (2H, m), 7.71-7.53 (3H, m), 7.42 (1H, d,  
J=8.9 Hz), 7.35 (1H, d, J=8.9 Hz), 7.22 (1H, s).

**STEP 4. Diethyl α-acetoxy-(2-benzoyl-4,5-dichloro-1H-indol-3-yl)malonate**

15 The title compound was prepared according to the procedure described in step 4  
of Example 2 (Method B) from 2-benzoyl-4,5-dichloroindole (step 3).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.85 (1H, br s), 7.91-7.86 (2H, m), 7.66-7.58 (1H, m), 7.52-7.44  
(2H, m), 7.36 (1H, d, J=8.7 Hz), 7.21 (1H, d, J=8.7 Hz), 4.20-3.98 (4H, m), 2.07 (3H,  
s), 1.15 (6H, t, J=7.3 Hz).

20 **STEP 5. Diethyl (2-benzoyl-4,5-dichloro-1H-indol-3-yl)malonate**

The title compound was prepared according to the procedure described in step 5  
of Example 2 (Method B) from diethyl α-acetoxy-(2-benzoyl-4,5-dichloro-1H-indol-3-  
yl)malonate (step 4).

25 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.24 (1H, br s), 7.82-7.76 (2H, m), 7.65-7.58 (1H, m), 7.55-7.44  
(2H, m), 7.20 (1H, d, J=8.7 Hz), 7.03 (1H, d, J=8.7 Hz), 5.89 (1H, s), 4.16-4.02 (4H,  
m), 1.20 (6H, t, J=7.3 Hz).

**STEP 6. (2-Benzoyl-4,5-dichloro-1H-indol-3-yl)acetic acid**

30 The title compound was prepared according to the procedure described in step 6  
of Example 2 (Method B) from diethyl (2-benzoyl-4,5-dichloro-1H-indol-3-  
yl)malonate (step 5).

m.p.: 249-252 °C (recrystallized from ethyl acetate/hexane).

IR (KBr)  $\nu$ : 1701, 1625, 1523, 1450, 1330, 1257, 1012 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 9.92 (1H, br s), 7.85-7.81 (2H, m), 7.66-7.42 (3H, m), 7.36 (1H, d, J=8.8 Hz), 7.29 (1H, d, J=8.8 Hz), 4.09 (2H, s).

5 **EXAMPLE 26**

**(2-BENZOYL-4,6-DICHLORO-1H-INDOL-3-YL)ACETIC ACID**

**STEP 1. 4,6-Dichloro-2-(N-methoxy-N-methylamino)carbonyl]indole**

The title compound was prepared according to the procedure described in step 1 of Example 7 from 4,6-dichloroindole-2-carboxylic acid (Salituro, Francesco G. et al., 10 *J. Med. Chem.*, 1990, 33, 2944).

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 12.09 (1H, br s), 7.48 (1H, dd, J=1.0, 1.6 Hz), 7.25 (1H, d, J=1.6 Hz), 7.11 (1H, s), 3.82 (3H, s), 3.63 (3H, s).

**STEP 2. 2-Benzoyl-4,6-dichloroindole**

The titled compound was prepared according to the procedure described in step 15 2 of Example 17 from 4,6-dichloro-2-[N-methoxy-N-methylamino)carbonyl]indole (step 1) and phenyllithium.

m.p.: 214-218 °C.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 9.45 (1H, br s), 8.02-7.95 (2H, m), 7.70-7.52 (3H, m), 7.40 (1H, d, J=1.6 Hz), 7.25 (1H, s), 7.20 (1H, d, J=1.6 Hz).

20 **STEP 3. Diethyl  $\alpha$ -acetoxy-(2-benzoyl-4,6-dichloro-1H-indol-3-yl)malonate**

The title compound was prepared according to the procedure described in step 4 of Example 2 (Method B) from 2-benzoyl-4,6-dichloroindole (step 2).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 8.92 (1H, br s), 7.95-7.86 (2H, m), 7.68-7.43 (3H, m), 7.29 (1H, d, J=1.8 Hz), 7.23 (1H, d, J=1.8 Hz), 4.60-4.00 (4H, m), 2.04 (3H, s), 1.30-1.10 (6H, m)

25 **STEP 4. Diethyl (2-benzoyl-4,6-dichloro-1H-indol-3-yl)malonate**

The title compound was prepared according to the procedure described in step 5 of Example 2 (Method B) from diethyl  $\alpha$ -acetoxy-(2-benzoyl-4,6-dichloro-1H-indol-3-yl)malonate (step 3).

m.p.: 170-172 °C.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.15 (1H, br s), 7.84-7.75 (2H, m), 7.66-7.45 (3H, m), 7.26 (1H, s), 7.12 (1H, s), 5.79 (1H, s), 4.20-4.00 (4H, m), 1.20 (6H, t, J=7.3 Hz).

**STEP 5. (2-Benzoyl-4,6-dichloro-1H-indol-3-yl)acetic acid**

The title compound was prepared according to the procedure described in step 6  
5 of Example 2 (Method B) from diethyl [2-benzoyl-4,5-dichloro-1H-indol-3-yl]malonate (step 4).

m.p.: 239-243 °C (recrystallized from ethyl acetate/hexane).

IR (KBr) v: 1725, 1555, 1525, 1330, 1287, 1250, 1005 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.40 (1H, br s), 12.12 (1H, br s), 7.80-7.67 (3H, m), 7.64-  
10 7.54 (2H, m), 7.48 (1H, d, J=1.8 Hz), 7.23 (1H, d, J=1.8 Hz), 3.99 (2H, s).

**EXAMPLE 27**

**(2-BENZOYL-5,6-DICHLORO-1H-INDOL-3-YL)ACETIC ACID**

**STEP 1. 5,6-dichloroindole-2-carboxylic acid**

The title compound was prepared according to the procedure described in step 1  
15 of Example 25 from ethyl 5,6-dichloroindole-2-carboxylate (Ishii et al., *Chem. Pharm. Bull.*, 1974, 22, 1981).

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.06 (1H, br s), 7.95 (1H, s), 7.62 (1H, s), 7.09 (1H, s).

**STEP 2. 5,6-Dichloro-2-[N-methoxy-N-methylamino)carbonyl]indole**

The title compound was prepared according to the procedure described in step 1  
20 of Example 7 from 5,6-dichloroindole-2-carboxylic acid (step 1).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 11.86 (1H, br s), 7.96 (1H, s), 7.66 (1H, s), 7.16 (1H, s), 3.80 (3H, s), 3.34 (3H, s).

**STEP 3. 2-Benzoyl-5,6-dichloroindole**

The titled compound was prepared according to the procedure described in step  
25 2 of Example 17 from 5,6-dichloro-2-[N-methoxy-N-methylamino)carbonyl]indole  
(step 2) and phenyllithium.

m.p.: 206-210 °C (recrystallized from ethyl acetate/hexane).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.35 (1H, br s), 8.00-7.93 (2H, m), 7.81 (1H, s), 7.69-7.51 (3H, m), 7.26 (1H, s), 7.08 (1H, s).

**30 STEP 4. Diethyl α-acetoxy-(2-benzoyl-5,6-dichloro-1H-indol-3-yl)malonate**

The title compound was prepared according to the procedure described in step 4 of Example 2 (Method B) from 2-benzoyl-5,6-dichloroindole (step 3).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.76 (1H, br s), 8.05 (1H, s), 7.90-7.82 (2H, m), 7.67-7.59 (1H, m), 7.54-7.44 (3H, m), 4.30-4.10 (4H, m), 1.69 (3H, s), 1.35-1.20 (6H, m).

5 **STEP 5. Diethyl (2-benzoyl-5,6-dichloro-1H-indol-3-yl)malonate**

The title compound was prepared according to the procedure described in step 5 of Example 2 (Method B) from diethyl α-acetoxy-(2-benzoyl-5,6-dichloro-1H-indol-3-yl)malonate (step 4).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.90 (1H, br s), 7.95 (1H, s), 7.82-7.76 (2H, m), 7.70-7.61 (1H, m), 7.58-7.46 (3H, m), 5.26 (1H, s), 4.30-4.05 (4H, m), 1.24 (6H, t, J=7.1 Hz).

**STEP 6. (2-Benzoyl-5,6-dichloro-1H-indol-3-yl)acetic acid**

The title compound was prepared according to the procedure described in step 6 of Example 2 (Method B) from diethyl (2-benzoyl-4,5-dichloro-1H-indol-3-yl)malonate (step 5).

15 m.p.: 208-210 °C (recrystallized from ethyl acetate/hexane).

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.91 (1H, br s), 8.04 (1H, s), 7.77-7.50 (6H, m), 3.81 (2H, s).

**EXAMPLE 28**

**dl-2-(2-BENZOYL-6-CHLORO-1H-INDOL-3-YL)PROPANOIC ACID**

**STEP 1. Diethyl α-methyl-(2-benzoyl-6-chloro-1H-indol-3-yl)malonate**

20 The title compound was prepared according to the procedure described in step 4 of Example 2 (Method B) from 2-benzoyl-6-chloroindole (step 3 of Example 1, Method B) and diethyl methylmalonate.

m.p.: 193-196 °C.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.42 (1H, br s), 7.87 (2H, m), 7.66-7.48 (3H, m), 7.42 (1H, d, J=8.8 Hz), 7.35 (1H, d, J=1.8 Hz), 7.11 (1H, dd, J=1.8, 8.8 Hz), 4.30-4.02 (4H, m), 1.98 (3H, s), 1.15 (6H, t, J=7.1 Hz).

**STEP 2. dl-2-(2-Benzoyl-6-chloro-1H-indol-3-yl)propanoic acid**

The title compound was prepared according to the procedure described in step 6 of Example 2 (Method B) from diethyl α-methyl-(2-benzoyl-6-chloro-1H-indol-3-yl)malonate (step 1).

m.p.: 204-208 °C (recrystallized from dichloromethane/hexane).

IR (KBr)  $\nu$ : 1720, 1620, 1475, 1260, 1230  $\text{cm}^{-1}$ .

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 12.29 (1H, br s), 11.72 (1H, br s), 7.82-7.76 (2H, m), 7.75-7.68 (2H, m), 7.65-7.57 (2H, m), 7.48 (1H, d, J=1.8 Hz), 7.12 (1H, dd, J=1.8, 8.4 Hz), 5 4.15 (1H, q, J=7.1 Hz), 1.44 (3H, d, J=7.1 Hz).

#### EXAMPLE 29 and EXAMPLE 30

less polar antipode, 2-(2-BENZOYL-6-CHLORO-1H-INDOL-3-YL)PROPANOIC ACID (EXAMPLE 29) and more polar antipode, 2-(2-BENZOYL-6-CHLORO-1H-INDOL-3-YL)PROPANOIC ACID (EXAMPLE 30)

10 Chiral separation of *dl*-2-(2-Benzoyl-6-chloro-1H-indol-3-yl)propanoic acid (Example 28) was performed by DAICEL CHIRALCEL OJ (4.6 x 250 mm, eluent: hexane/isopropanol/trifluoroacetic acid = 85:15:0.1, flow rate: 1.0 ml/min) to afford; less polar compound (retention time: 17 min.) and more polar compound (retention time: 27 min.).

15 EXAMPLE 31

[6-CHLORO-2-(4-METHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

STEP 1. Methyl *trans*-4-chloro-2-(ethoxycarbonylamino)cinnamate

To a stirred solution of methyl *trans*-2-amino-4-chlorocinnamate (R.W.Carling 20 et al., *J.Med.Chem.*, 1993, 36, 3397., 32.6 g, 0.15 mol), pyridine (14.9 ml, 0.17 mol) and 4-dimethylaminopyridine (0.5 g) in dichloromethane (500 ml) was added dropwise ethyl chloroformate (16.2 ml, 0.17 mol) at room temperature. After stirring for 2h, the mixture was concentrated. The residue was diluted in ethyl acetate (1000ml) and washed with 10% aqueous citric acid (500ml). The organic layer was successively 25 washed with water (500 ml), saturated sodium bicarbonate (500 ml), water (500 ml), brine (500 ml). After drying ( $\text{MgSO}_4$ ) and removal of solvent, the residual solids were recrystallized from ethyl acetate/hexane to give 39.13 g (92 %) of the title compound.

<sup>1</sup>H-NMR ( $\text{CDCl}_3$ )  $\delta$ : 7.95 (1H, br s), 7.76 (1H, d, J=15.8Hz), 7.42 (1H, d, J=8.6Hz), 30 7.22 (1H, dd, J=2.1, 8.5Hz), 6.69 (1H, br), 6.37 (1H, d, J=15.7Hz), 4.26 (2H, q, J=7.3Hz), 3.82 (3H, s), 1.34 (3H, t, J=7.25Hz).

STEP 2. Methyl [6-chloro-1-ethoxycarbonyl-2-(4-methylpyridine-2-carbonyl)indolin-3-yl]acetate

A mixture of methyl *trans*-4-chloro-2-(ethoxycarbonylamino)cinnamate (step 1, 1.5 g, 5.3 mmol), 2-bromoacetyl-4-methylpyridine hydrobromide\*, potassium carbonate (7.3 g, 53 mmol) and acetonitrile (50 ml) was heated at reflux temperature for 17h. The mixture was then cooled and concentrated. The residue was diluted in ethyl acetate (200 ml) and washed with water (200 ml) and brine (200 ml). After drying ( $\text{MgSO}_4$ ) and removal of solvent, the crude product was purified by flash column chromatography eluting with ethyl acetate/hexane (1:5) to afford 433 mg (20 %) of the title compound.

MS (EI) m/z: 416 ( $\text{M}^+$ ).

\* 2-bromoacetyl-4-methylpyridine hydrobromide was prepared as follows;

To a stirred solution of 2-acetyl-4-methylpyridine (F.H.Case et al, *J. Am. Chem. Soc.*, 1956, 78, 5842., 7.8 g, 57.7 mmol) in 25% HBr-AcOH (40 ml) was added dropwise a solution of bromine (10.1 g, 63.5 mmol) in AcOH (10 ml) with ice-cooling. After stirring for 1h, diethyl ether (100 ml) was added and the precipitates were collected by filtration to give 10.8 g (63 %) of the title compound.

$^1\text{H-NMR}$  (DMSO-d<sub>6</sub>) d: 8.71 (1H, d, J=5.1Hz), 8.14 (1H, s), 7.75 (1H, d, J=5.1Hz), 5.07 (2H, s), 2.52 (3H, s).

STEP 3. [6-Chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid

A stirred solution of methyl [6-chloro-1-ethoxycarbonyl-2-(4-methylpyridine-2-carbonyl)indolin-3-yl]acetate (step 2, 930 mg, 2.2 mmol) in ethanol (20 ml) and 2N aqueous NaOH (10 ml) was heated at reflux temperature for 72h. After cooling to room temperature, the resulting mixture was neutralized with 2N aqueous HCl (10 ml) and concentrated. The residue was diluted in dichloromethane/methanol (10:1, 300 ml) and dried ( $\text{MgSO}_4$ ). After removal of solvent, the crude product was purified by flash column chromatography eluting with dichloromethane/methanol (20:1) and then washed with i-PrOH (ca.20 ml) to give 120 mg (17 %) of the title compound as a yellow powder.

m.p.: 223 °C (decomposed).

IR (KBr) v: 1707, 1647, 1595, 1533, 1487, 1429, 1276, 1289, 1196  $\text{cm}^{-1}$ .

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.30 (1H, s), 8.70 (1H, d, J=4.9Hz), 7.96 (1H, br s), 7.85-7.70 (2H, m), 7.65-7.55 (1H, m), 7.17-7.07 (1H, m), 4.08 (2H, s), 2.47 (3H, s).

### **EXAMPLE 32**

#### **[6-CHLORO-2-(5-METHYL PYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

##### **STEP 1. Methyl [6-chloro-1-ethoxycarbonyl-2-(5-methylpyridine-2-carbonyl)indolin-3-yl]acetate**

Two diastereomers of the title compound were prepared according the procedure described in step 2 of Example 31 from methyl *trans*-4-chloro-2-(ethoxycarbonylamino)cinnamate (Example 31, step 1) and 2-bromoacetyl-5-methylpyridine.\*

Less polar product; tlc: Rf=0.30 (ethyl acetate/hexane=1/2), MS (EI) m/z: 416 (M<sup>+</sup>).

More polar product; tlc: Rf=0.25 (ethyl acetate/hexane=1/2), MS (EI) m/z: 416 (M<sup>+</sup>).

\* 2-Bromoacetyl-5-methylpyridine was prepared as follows;

A mixture of 2-bromo-5-methylpyridine (5.00 g, 29.06 mmol), tributyl(1-ethoxyvinyl)tin (10.49 g, 29.07 mmol), and tetrakis(triphenylphosphine)palladium (3.36 g, 2.91 mmol) in toluene (40 ml) was heated at reflux temperature for 18 h. The mixture was cooled, filtered through a pad of Celite and then concentrated. The residue (~10 g) was dissolved in a mixture of THF (100 ml) and water (20 ml), cooled to 0 °C and *N*-bromosuccinimide (5.43 g, 30.52 mmol) was added over 20 min. The resulting mixture was stirred for 0.5 h at the same temperature and then concentrated to ca. 20 ml. The mixture was diluted in ethyl acetate (300 ml), washed with water (100 ml x 3), and dried (MgSO<sub>4</sub>). After removal of solvent, the crude product was purified by flash column chromatography eluting with ethyl acetate/hexane (1:15 to 1:10) to afford 2.30 g (37%) of the title compound as an oil.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.49 (1 H, br s), 8.01 (1 H, d, J=8.1 Hz), 7.68-7.64 (1 H, m), 4.84 (2 H, s), 2.44 (3 H, s).

##### **STEP 2. [6-Chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid**

Both of the diastereoisomers of methyl [6-chloro-1-ethoxycarbonyl-2-(5-methylpyridine-2-carbonyl)indolin-3-yl]acetate (step 2) were converted to the title compound, respectively, according to the procedure described in step 3 of Example 31.

MS (EI) m/z: 328 ( $M^+$ )

m.p.: 235-238 °C (recrystallized from ethyl acetate).

IR (KBr)  $\nu$ : 3281, 1699, 1638, 1529, 1310, 1150, 797, 702  $\text{cm}^{-1}$ .

$^1\text{H-NMR}$  (DMSO-d<sub>6</sub>)  $\delta$ : 12.26 (1 H, br s), 8.68 (1 H, br s), 8.04 (1 H, d,  $J=8.1$  Hz),

- 5 7.94 (1 H, br d,  $J=9.1$  Hz), 7.79 (1 H, d,  $J=8.7$  Hz), 7.74 (1 H, br s), 7.11 (1 H, br d,  $J=8.6$  Hz), 4.10 (2 H, s), 2.47 (3 H, s). One signal due to NH or COOH was not observed.

### EXAMPLE 33

METHYL [6-CHLORO-2-(4-CHLOROPYRIDINE-2-CARBONYL)-1H-INDOL-3-

10 YL]ACETATE

A mixture of methyl *trans*-4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of Example 8; Method A, 675 mg, 1.92 mmol), 2-bromoacetyl-4-chloropyridine hydrobromide\* (907 mg, 2.88 mmol), and potassium carbonate (2.65 g, 19.18 mmol) in acetone (20 ml) was heated at reflux temperature for 4 h. The mixture was cooled 15 and concentrated. The residue was diluted with ethyl acetate (150 ml) and washed with water (70 ml x 6). After drying ( $\text{MgSO}_4$ ) and removal of solvent, the crude product was purified by flash column chromatography eluting with ethyl acetate/hexane (1:6-1:3) to afford 195 mg (28%) of the title compound (yellow solids) along with 264 mg (27%) of methyl [6-chloro-2-(4-chloropyridine-2-carbonyl)-16 phenylsulfonyl]indolin-3-yl]acetate (brown crystals).

Methyl [6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate:

MS (EI) m/z : 362 ( $M^+$ ).

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 12.09 (1 H, br s), 8.62 (1 H, d,  $J=5.3$  Hz), 8.28 (1 H, d,  $J=2.1$  Hz),

7.57 (1 H, d,  $J=8.6$  Hz), 7.52 (1 H, dd,  $J=2.0$  and 5.3 Hz), 7.45 (1 H, d,  $J=1.8$  Hz), 7.08

- 25 (1 H, dd,  $J=1.8$  and 8.7 Hz), 4.27 (2 H, s), 3.75 (3 H, s).

Methyl [6-chloro-2-(4-chloropyridine-2-carbonyl)-1-(phenylsulfonyl)indolin-3-yl]acetate:

tlc:  $R_f=0.35$  (ethyl acetate/hexane=1:2).

MS (EI) m/z (intensity): 504 ( $M^+$ , 0.1), 363 (90), 335 (30), 304 (100), 275 (10), 223

- 30 (15).

\* 2-Bromoacetyl-4-chloropyridine hydrobromide was prepared as follows;

4-Chloro-2-pyridinecarbonitrile: To a mixture of 4-chloropyridine-*N*-oxide (5.00 g, 38.6 mmol) and trimethylsilyl cyanide (4.84 g, 46.3 mmol) in dichloromethane (60 ml) cooled to 0 °C was added dropwise *N,N*-dimethylcarbamoyl chloride (3.8 ml, 40.5 mmol). The mixture was allowed to warm to ambient temperature and stirred for 16 h. The mixture was cooled to 0 °C and a 30% aqueous solution of potassium carbonate (100 ml) was added. The crude product was extracted with dichloromethane (100 ml x 2), the organic extracts dried ( $\text{MgSO}_4$ ) and evaporated to give 4-chloro-2-pyridinecarbonitrile (5.35 g, 100%).

10       $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.63 (1 H, d,  $J=4.8$  Hz), 7.72 (1 H, d,  $J=2.6$  Hz), 7.55 (1 H, dd,  $J=1.8, 5.1$  Hz).

2-Acetyl-4-chloropyridine: To a solution of 4-chloro-2-pyridinecarbonitrile (5.35 g, 38.6 mmol) in benzene (50 ml) and ether (50 ml) cooled to 0 °C was added dropwise over 20 min a 2M solution of  $\text{MeMgI}$  in ether (23 ml, 46.3 mmol). After 0.5 h, the mixture was allowed to warm to ambient temperature, and stirring continued for 2 h. The mixture was cooled to 0 °C and 2M aqueous  $\text{HCl}$  (100 ml) added. The mixture was made basic with saturated aqueous sodium bicarbonate (~80 ml) and the organic layer separated and dried ( $\text{MgSO}_4$ ). After removal of solvent, the residue was purified by flash chromatography eluting with ethyl acetate/hexane (1:5) to afford 3.60 g (60%) of 2-acetyl-4-chloropyridine.

20       $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$ : 8.59 (1 H, d,  $J=5.1$  Hz), 8.04 (1 H, d,  $J=1.8$  Hz), 7.47 (1 H, dd,  $J=1.8, 5.1$  Hz), 2.72 (3 H, s).

2-Bromoacetyl-4-chloropyridine hydrobromide: 2-(Bromoacetyl)-4-chloropyridine hydrobromide was prepared from 2-acetyl-4-chloropyridine according to the method of H. McKennis, Jr., L. B. Turnbull, E. R. Bowman, and E. Tamaki (in *J. Org. Chem.*, 25 **1963**, 28, 383-387).

$^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$ : 8.74 (1 H, d,  $J=5.5$  Hz), 8.05 (1 H, d,  $J=1.8$  Hz), 7.88 (1 H, dd,  $J=2.2$  and 5.5 Hz), 5.02 (2 H, s).

#### EXAMPLE 34

30      [6-CHLORO-2-(4-CHLOROPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

A suspension of methyl [6-chloro-2-[4-chloropyridine-2-carbonyl]-1H-indol-3-

yl]acetate (Example 33, 195 mg, 0.537 mmol) in ethanol (20 ml) and 2N sodium hydroxide (4 ml) was heated for 1 h at 50 °C. After cooling to room temperature, 2N hydrochloric acid (4 ml) was added and the mixture was concentrated. The residue was diluted in ethyl acetate (100 ml), washed with water (50 ml x 2), and dried (MgSO<sub>4</sub>). After removal of solvent, the crystalline residue was recrystallized from ethyl acetate to afford 175 mg (94%) of the title compound.

5 m.p.: 233-234 °C.

IR (KBr) v: 3306, 1709, 1641, 1531, 1254, 1236, 741 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.20 (1 H, br s), 12.16 (1 H, br s), 8.80 (1 H, d, J=5.4 Hz),  
10 8.12 (1 H, d, J=2.1 Hz), 7.90 (1 H, dd, J=2.1, 5.3 Hz), 7.81 (1 H, d, J=8.7 Hz), 7.70 (1  
H, d, J=1.8 Hz), 7.13 (1 H, dd, J=2.0, 8.7 Hz), 4.07 (2 H, s).

### EXAMPLE 35

#### [6-CHLORO-2-(PYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

STEP 1. Methyl [6-chloro-1-ethoxycarbonyl-2-(pyridine-2-carbonyl)indolin-3-yl]acetate

The title compound were prepared according the procedure described in step 1 of Example 31 from methyl *trans*-4-chloro-2-(ethoxycarbonylamino)cinnamate (Example 31, step 1) and 2-bromoacetylpyridine hydrobromide (H.McKennis et al. *J.Org.Chem.*, 1963, 387.).

20 tlc: R<sub>f</sub>=0.3 (ethyl acetate/hexane=1:3).

#### STEP 2. [6-Chloro-2-(pyridine-2-carbonyl)-1H-indol-3-yl]acetic acid

The title compound were prepared according the procedure described in step 3 of Example 31 from methyl [6-chloro-1-ethoxycarbonyl-2-(pyridine-2-carbonyl)indolin-3-yl]acetate (step 1).

25 m.p.: 210 °C (decomposed).

IR (KBr) v: 3280, 1697, 1643, 1531, 1234, 1150 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.22 (1H, s), 8.84 (1H, d, J=4.9Hz), 8.15-8.05 (2H, m), 7.85-  
7.65 (3H, m), 7.11 (1H, dd, J=1.9, 8.7Hz), 4.04 (2H, s).

### EXAMPLE 36

30 [5-CHLORO-2-(4-METHYL PYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

STEP 1. Methyl *trans*-5-chloro-2-nitrocinnamate

A mixture of the 5-chloro-2-nitrobenzaldehyde (9.68 g, 52.16 mmol) and methyl (triphenylphosphoranylidene)acetate (18.31 g, 54.77 mmol) in toluene (200 ml) was heated at reflux temperature for 2 h. The mixture was concentrated and the crystalline residue was purified by flash column chromatography eluting with ethyl acetate/hexane (1:5) to afford crystals. Recrystallization from ethyl acetate/hexane gave 7.54 g (60%) of the title compound as pale yellow solids.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.09 (1 H, d, J=15.8 Hz), 8.04 (1 H, d, J=8.7 Hz), 7.60 (1 H, d, J=2.1 Hz), 7.51 (1 H, dd, J=2.1, 8.7 Hz), 6.36 (1 H, d, J=15.8 Hz), 3.84 (3 H, s).

10 STEP 2. Methyl *trans*-2-amino-5-chlorocinnamate

A mixture of methyl *trans*-5-chloro-2-nitrocinnamate (step 1, 3.00 g, 12.42 mmol), iron powder (3.65 g, 62.08 mmol), ammonium chloride (332 mg, 6.21 mmol), ethanol (60 ml) and water (10 ml) was heated at reflux temperature for 2 h. The mixture was cooled and filtered through a pad of Celite. The filtrate was concentrated. The residue was diluted with ethyl acetate (200 ml) and washed with water (100 ml x 2). After drying (MgSO<sub>4</sub>), removal of solvent gave 2.57 g (98%) of the title compound as crystals.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.73 (1 H, d, J=15.8 Hz), 7.34 (1 H, d, J=2.5 Hz), 7.12 (1 H, dd, J=2.3, 8.6 Hz), 6.64 (1 H, d, J=8.6 Hz), 6.35 (1 H, d, J=15.8 Hz), 3.95 (2 H, br s), 3.81 (3 H, s).

20 STEP 3. Methyl *trans*-5-chloro-2-(phenylsulfonylamino)cinnamate

The title compound was prepared according to the procedure described in step 1 of Example 8 (Method A) from methyl *trans*-2-amino-5-chlorocinnamate (step 2).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.72-7.67 (2 H, m), 7.58-7.51 (1 H, m), 7.47-7.40 (4 H, m), 7.36 (1 H, d, J=8.6 Hz), 7.31 (1 H, dd, J=2.1, 8.6 Hz), 6.14 (1 H, d, J=15.8 Hz), 3.78 (3 H, s). One signal due to NH was not observed.

25 STEP 4. Methyl [5-Chloro-2-(4-methylpyridine-2-carbonyl)-1-(phenylsulfonyl)indolin-3-yl]acetate

The title compound was prepared according to the procedure described in step 2 of Example 8 (Method A) from methyl *trans*-5-chloro-2-(phenylsulfonylamino)cinnamate (step 3) and 2-bromoacetyl-4-methylpyridine

hydrobromide (F.H.Case et al., *J.Am.Chem.Soc.*, **1956**, 78, 5842).

tlc: R<sub>f</sub>=0.32 (ethyl acetate/hexane=1:2)

**STEP 5. [5-Chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid**

The title compound was prepared according to the procedure described in step 3  
5 of Example 31 from methyl [5-chloro-2-(4-methylpyridine-2-carbonyl)-1-  
(phenylsulfonyl)indolin-3-yl]acetate (step 4).

MS (EI) m/z: 328 (M<sup>+</sup>).

m.p.: 230-231 °C (recrystallized from ethyl acetate).

IR (KBr) v: 3292, 1699, 1597, 1533, 1282, 1198, 1059, 802, 704 cm<sup>-1</sup>.

10 <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.26 (1 H, br s), 8.69 (1 H, d, J=5.1 Hz), 7.93 (1 H, br s),  
7.82 (1 H, d, J=2.0 Hz), 7.66 (1 H, d, J=8.7 Hz), 7.56 (1 H, br d, J=4.9 Hz), 7.31 (1 H,  
dd, J=2.0, 8.7 Hz), 4.02 (2 H, s), 2.46 (3 H, s). One signal due to NH or COOH was  
not observed.

**EXAMPLE 37**

15 **METHYL [5-CHLORO-2-(6-METHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE**

**STEP 1. Methyl [5-chloro-2-(6-methylpyridine-2-carbonyl)-1-(phenylsulfonyl)indolin-3-yl]acetate**

The title compound was prepared according to the procedure described in step 3  
20 of Example 8 (Method A) from methyl *trans*-5-chloro-2-(phenylsulfonylamino)cinnamate (Example 36, step 3) and 2-bromoacetyl-6-methylpyridine hydrobromide (H.Erlenmeyer, J.Jenni, and B.Pras.  
*J.Med.Pharm.Chem.*, **1961**, 3, 561-566).

tlc: R<sub>f</sub>=0.39 (ethyl acetate/hexane=2:3).

25 **STEP 2. Methyl [5-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate**

The title compound was prepared according to the procedure described in step 3  
of Example 8 (Method A) from methyl [5-chloro-2-(6-methylpyridine-2-carbonyl)-1-  
(phenylsulfonyl)indolin-3-yl]acetate (step 1).

1 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.62 (1 H, br s), 8.15 (1 H, d, J=7.9 Hz), 7.84 (1 H, t, J=7.7 Hz),  
30 7.67 (1 H, d, J=1.8 Hz), 7.43 (1 H, d, J=8.9 Hz), 7.40 (1 H, d, J=7.7 Hz), 7.32 (1 H, dd,  
J=2.0, 8.7 Hz), 4.28 (2 H, s), 3.73 (3 H, s), 2.76 (3 H, s).

**Example 38****[5-CHLORO-2-(6-METHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in  
5 Example 34 from methyl [5-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate.

MS (EI) m/z: 328 ( $M^+$ ).

m.p.: 225-226°C (recrystallized from ethyl acetate).

IR (KBr)  $\nu$ : 1705, 1636, 1529, 1333, 1236, 1180, 1061, 669  $\text{cm}^{-1}$ .

10  $^1\text{H-NMR}$  (DMSO-d<sub>6</sub>)  $\delta$ : 12.13 (1 H, br s), 12.09 (1 H, br s), 7.99 (1 H, t, J=7.7 Hz),  
7.87 (1 H, d, J=7.7 Hz), 7.84 (1 H, d, J=2.0 Hz), 7.66 (1 H, d, J=8.9 Hz), 7.59 (1 H, d,  
J=7.6 Hz), 7.33 (1 h, dd, J=2.0, 8.9 Hz), 4.03 (2 H, s), 2.69 (3 H, s).

**EXAMPLE 39****[6-CHLORO-2-(1-METHYLMIDAZOLE-2-CARBONYL)-1H-INDOL-3-**

15 **YL]ACETIC ACID**

**STEP 1. Methyl [6-chloro-1-ethoxycarbonyl-2-(1-methylimidazole-2-carbonyl)indolin-3-yl]acetate**

The title compound was prepared according to the procedure described in step 2  
of Example 31 from methyl *trans*-4-chloro-2-(ethoxycarbonylamino)cinnamate  
20 (Example 31, step 1) and 2-bromoacetyl-1-methylimidazole hydrobromide.\*

MS (EI) m/z: 405 ( $M^+$ ).

\* 2-Bromoacetyl-1-methylimidazole hydrobromide was prepared as follows;

To a stirred suspension of 2-acetyl-1-methylimidazole (D.H.Davis, J.Hall, and  
E.H.Smith, *J.Chem.Soc.Perkin trans. 1*, 1991, 2691., 3.0 g, 26.8 mmol) in 25% HBr-  
25 AcOH was added dropwise a solution of bromine (4.7 g, 29.5 mmol) with ice-cooling.  
After stirring for 0.5h, the mixture was allowed to warm to room temperature and the  
stirring was continued for an additional 1h. To the mixture was added diethyl ether  
(150 ml) and the mixture was cooled with ice-bath. The precipitates were collected  
by filtration to give 5.2 g (66 %) of the title compound as a pale yellow powder.

30  $^1\text{H-NMR}$  (DMSO-d<sub>6</sub>) d: 7.61 (1H, s), 7.27 (1H, s), 4.68 (2H, s), 3.81 (3H, s).

**STEP 2. [6-Chloro-2-(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetic acid**

The title compound was prepared according to the procedure described in step 3 of Example 31 from [6-chloro-1-ethoxycarbonyl-2-(1-methylimidazole-2-carbonyl)indolin-3-yl]acetate (step 1).

m.p.: 236 °C (decomposed).

5 MS (EI) m/z: 317 ( $M^+$ ).

IR (KBr)  $\nu$ : 3238, 1695, 1630, 1537, 1402, 1229, 1146  $\text{cm}^{-1}$ .

$^1\text{H-NMR}$  ( $\text{CDCl}_3+\text{DMSO-d}_6$ )  $\delta$ : 12.30 (1H, s), 7.65 (1H, d,  $J=8.7\text{Hz}$ ), 7.50 (1H, d,  $J=1.8\text{Hz}$ ), 7.42 (1H, s), 7.28-7.23 (1H, m), 7.16 (1H, s), 7.09 (1H, dd,  $J=1.8, 8.6\text{Hz}$ ), 4.25 (2H, s), 4.13 (3H, s).

10 **EXAMPLE 40**

**METHYL [5-CHLORO-2-(THIAZOLE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE**

**STEP 1. Methyl [5-chloro-1-phenylsulfonyl-2-(thiazole-2-carbonyl)indolin-3-yl]acetate**

The title compound was prepared according to the procedure described in step 2 of Example 8 (Method A) from methyl *trans*-5-chloro-2-(phenylsulfonylamino)cinnamate (Example 36, step 3) and 2-bromoacetylthiazole hydrobromide (A.Dondoni, A.Marra, and P.Merino, *J.Am.Chem.Soc.*, **1994**, 116, 3324) tlc:  $R_f=0.07$  (ethyl acetate/hexane=1:2).

**STEP 2. Methyl [5-chloro-2-(thiazole-2-carbonyl)-1H-indol-3-yl]acetate**

20 The title compound was prepared according to the procedure described in step 3 of Example 8 (Method A) from methyl [5-chloro-1-phenylsulfonyl-2-(thiazole-2-carbonyl)indolin-3-yl]acetate (step 1).

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 11.78 (1 H, br s), 8.12 (1 H, d,  $J=3.1\text{ Hz}$ ), 7.75 (1 H, d,  $J=3.1\text{ Hz}$ ), 7.68 (1 H, d,  $J=1.8\text{ Hz}$ ), 7.44 (1 H, d,  $J=8.7\text{ Hz}$ ), 7.34 (1 H, dd,  $J=2.0, 8.9\text{ Hz}$ ), 4.29 (2 H, s), 3.74 (3 H, s).

**EXAMPLE 41**

**[5-CHLORO-2-(THIAZOLE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl [5-chloro-1-phenylsulfonyl-2-(thiazole-2-carbonyl)-1H-indol-3-yl]acetate (step 2).

MS (EI) m/z: 320 ( $M^+$ ).

m.p.; 230-231°C (recrystallized from ethyl acetate).

IR (KBr)  $\nu$ : 3302, 1703, 1636, 1541, 1387, 1335, 1267, 1232, 1186, 1003, 766  $\text{cm}^{-1}$ .

$^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$ : 12.23 (1 H, br s), 12.10 (1 H, br s), 8.33 (1 H, d,  $J=3.1$  Hz), 8.31 (1 H, d,  $J=3.1$  Hz), 7.89 (1 H, d,  $J=2.0$  Hz), 7.77 (1 H, d,  $J=8.9$  Hz), 7.36 (1 H, dd,

5  $J=2.0$ , 8.7 Hz), 4.17 (2 H, s).

#### EXAMPLE 42

##### METHYL (2-BENZOYL-6-CHLORO-1H-INDOL-3-YL)ACETATE

A mixture of (2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid (Example 2, 50 mg, 0.16 mmol) and 10% HCl in methanol (3 ml) was stirred for 3 h at room temperature.

10 The mixture was concentrated and the residue was purified by flash column chromatography eluting with ethyl acetate/hexane (1:5) to afford 23 mg (44 %) of the title compound as white solids.

m.p.: 134-137 °C.

IR (KBr)  $\nu$ : 1735, 1620, 1529, 1434, 1325, 1147, 1013, 945  $\text{cm}^{-1}$ .

15  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.96 (1H, br s), 7.85-7.74 (2H, m), 7.66-7.47 (4H, m), 7.38 (1H, d,  $J=1.8$  Hz), 7.15 (1H, dd,  $J=1.8$ , 8.6 Hz), 3.18 (2H, s), 3.65 (3H, s).

#### EXAMPLE 43

##### (2-BENZOYL-6-CHLORO-1H-INDOL-3-YL)-N,N-DIMETHYLACETAMIDE

To a solution of (2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid (Example 2, 140 mg, 0.45 mmol), dimethylamine hydrochloride (45 mg, 0.54 mmol) and triethylamine (0.1 ml, 0.54 mmol) in DMF (2 ml) at 0 °C was added diethyl phosphorocyanide (DEPC, 0.1 ml, 0.54 mmol). The mixture was then stirred at room temperature for 1 h. The mixture was poured into water (20 ml) and extracted with diethyl ether (50 ml x 2). The organic extracts were washed with water (30 ml x 2), dried ( $\text{MgSO}_4$ ) and 25 concentrated. The residual solids were recrystallized from ethyl acetate/hexane to afford 50 mg (33%) of the title compound.

m.p.: 190-193 °C (recrystallized from ethyl acetate/hexane).

IR (KBr)  $\nu$ : 1631, 1232, 1007, 908  $\text{cm}^{-1}$ .

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 11.72 (1H, br s), 7.72-7.64 (4H, m), 7.60-7.52 (2H, m), 7.45 (1H,

30 d,  $J=1.2$  Hz), 7.08 (1H, d,  $J=8.6$  Hz), 3.32 (2H, s), 2.80 (3H, s), 2.76 (3H, s).

**EXAMPLE 44****(2-BENZOYL-6-CHLORO-1H-INDOL-3-YL)-N-METHYLACETAMIDE**

The title compound was prepared according to the procedure described in Example 43 from (2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid (Example 2) and 5 methylamine hydrochloride.

m.p.: 242-246 °C (recrystallized from ethyl acetate/hexane).

IR (KBr) v: 1618, 1527, 1409, 1325 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 11.71 (1H, br s), 7.82-7.75 (2H, m), 7.62-7.52 (5H, m), 7.49-7.46 (1H, m), 7.15-7.08 (1H, m), 3.64 (2H, s), 3.31 (3H, s).

**EXAMPLE 45****(2-BENZOYL-6-CHLORO-1H-INDOL-3-YL)ACETAMIDE**

The title compound was prepared according to the procedure described in Example 43 from (2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid (Example 2) and a solution of ammonia in THF.

15 m.p.: 234-237 °C.

IR (KBr) v: 1665, 1618, 1566, 1523, 1325, 1259, 943 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 11.66 (1H, br s), 7.82-7.75 (2H, m), 7.74-7.65 (2H, m), 7.62-7.53 (2H, m), 7.46 (1H, d, J=1.8 Hz), 7.27 (1H, br s), 7.12 (1H, dd, J=1.8, 8.6 Hz), 6.85 (1H, br s), 3.63 (2H, s).

**EXAMPLE 46****(2-BENZOYL-6-CHLORO-1H-INDOL-3-YL)-N-METHOXY-N-METHYLACETAMIDE**

The title compound was prepared according to the procedure described in Example 43 from (2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid (Example 2) and N-(2-

25 dimethylhydroxylamine hydrochloride.

m.p.: 109.9 - 112.2 °C (decomposed).

IR (KBr) v: 3179, 2970, 2937, 1634, 1599, 1570 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.20 - 8.90 (1H, m), 7.84 - 7.75 (2H, m), 7.66 - 7.45 (4H, m), 7.33 (1H, d, J=1.3Hz), 7.12 (1H, dd, J=8.6, 1.8Hz), 3.94 (2H, s), 3.51 (3H,s), 3.13 (3H, s).

**EXAMPLE 47**

2-(2-BENZOYL-6-CHLORO-1H-INDOL-3-YL)-1-PIPERIDINO-1-ETHANONESTEP 1. 7-Chloro-1-phenyl-9*H*-pyrano[3,4-b]indole-3-one

A solution of (2-benzoyl-6-chloro-1*H*-indol-3-yl)acetic acid (Example 2, 200 mg, 0.64 mmol), diethyl phosphorocyanide (DEPC, 0.12 ml, 0.76 mmol) and triethylamine (0.11 ml, 0.76 mmol) in DMF (3.0 ml) was stirred at room temperature for 5 min. The mixture was then poured into water (20 ml) and the orange precipitates were collected by filtration to give 20 mg (11%) of the title compound as orange solids.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 10.79 (1H, br s), 8.10 (1H, d, J=8.4 Hz), 7.93-7.84 (2H, m), 7.67-10 7.50 (3H, m), 7.29 (1H, s), 7.13 (1H, d, J=8.4 Hz), 6.87 (1H, s).

STEP 2. 2-(2-Benzoyl-6-chloro-1*H*-indol-3-yl)-1-piperidino-1-ethanone

A mixture of 7-chloro-1-phenyl-9*H*-pyrano[3,4-b]indole-3-one (step 1, 0.30 g, 1.0 mmol), and piperidine (1.0 ml, 10 mmol) in methanol (20 ml) was heated under reflux temperature for 2 h. After cooling down to rt, the yellow mixture was concentrated and the residual solids were recrystallized from methanol/hexane to give 0.12 g (32 %) of the title compound.

m.p.:223-224 °C.

IR (KBr) ν: 3310, 2928, 1655, 1570, 1533, 1447, 1323, 1256, 1225, 1059, 945, 858, 737, 700 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.7 (1H, br s), 7.74-7.63 (4H, m), 7.55 (2H, t, J=8.7 Hz), 7.46 (1H, d, J=1.8 Hz), 7.09 (1H, dd, J=8.7, 1.8 Hz), 3.80 (2H, s), 3.45-3.20 (4H, m), 1.55-1.20 (6H, m)

EXAMPLE 482-(2-BENZOYL-6-CHLORO-1H-INDOL-3-YL)-N-(4-METHYL-1-PIPERAZINYL)-1-ETHANONE

The title compound was prepared according to the procedure described in Example 43 from (2-benzoyl-6-chloro-1*H*-indol-3-yl)acetic acid (Example 2) and 1-methylpiperazine.

m.p.: 184-185 °C (recrystallized from methanol/hexane).

IR (KBr) ν: 2939, 2795, 1634, 1531, 1435, 1325, 1229, 1144, 1001, 737, 700 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.37 (1H, br s), 7.78-7.75 (1H, m), 7.73 (1H, d, J=1.5 Hz), 7.62-

7.52 (2H, m), 7.52-7.43 (2H, m), 7.18-7.10 (1H, m), 7.10-7.02 (1H, m), 3.81 (2H, s), 3.54 (2H, br s), 3.36 (2H, t, J=4.8 Hz), 2.36-2.22 (4H, m), 2.28 (3H, s).

**EXAMPLE 49**

**(2-BENZOYL-6-CHLORO-1H-INDOL-3-YL)-N-(2-CYANOETHYL)ACETAMIDE**

5 The title compound was prepared according to the procedure described in Example 43 from (2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid (Example 2) and aminopropionitrile.

m.p.: 233-233.5 °C (recrystallized from methanol/hexane).

10  $^1\text{H-NMR}$  (DMSO-d<sub>6</sub>) δ: 11.7 (1H, br s), 8.16 (1H, t, J=6.3Hz), 7.81-7.75 (2H, m), 7.72-7.64 (2H, m), 7.62-7.53 (2H, m), 7.47 (1H, d, J=1.9 Hz), 7.10 (1H, dd, J=8.7, 1.9 Hz), 3.67 (2H, s), 3.23 (2H, q, J=6.3 Hz), 2.58 (2H, t, J=6.3 Hz)

**EXAMPLE 50**

**(2-BENZOYL-6-CHLORO-1H-INDOL-3-YL)-N-(2-HYDROXYETHYL)ACETAMIDE**

15 The title compound was prepared according to the procedure described in Example 43 from (2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid (Example 2) and 2-aminoethanol.

m.p.: 178-179.5 °C (recrystallized from methanol/hexane).

20  $^1\text{H-NMR}$  (DMSO-d<sub>6</sub>) δ: 11.7 (1H, br s), 7.84-7.75 (3H, m), 7.72-7.64 (2H, m), 7.52 (2H, m), 7.46 (1H, d, J=2.0 Hz), 7.11 (1H, dd, J=8.6, 2.0 Hz), 3.64 (2H, s), 3.38 (3H, m), 3.06 (2H, q, J=5.9 Hz).

**EXAMPLE 51**

**2-(2-BENZOYL-6-CHLORO-1H-INDOL-3-YL)-1-MORPHOLINO-1-ETHANONE**

The title compound was prepared according to the procedure described in  
25 Example 43 from (2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid (Example 2) and morpholine.

m.p.: 187.7-189.5 °C.

IR (KBr) v: 3339, 2964, 2849, 1653, 1612, 1568 cm<sup>-1</sup>.

30  $^1\text{H-NMR}$  (CDCl<sub>3</sub>) δ: 9.08 - 8.92 (1H, m), 7.81 - 7.72 (2H, m), 7.69 - 7.58 (2H, m), 7.56 - 7.47 (2H, m), 7.29 (1H, d, J=1.8Hz), 7.12 (1H, dd, J=8.6, 1.8Hz), 3.87 (2H, s), 3.67 - 3.46 (6H, m), 3.41 - 3.31 (2H, m).

**EXAMPLE 52****[2-(4-CHLOROBENZOYL)-1H-INDOL-3-YL]ACETIC ACID****STEP 1. 2-(4-Chlorobenzoyl)-1-(phenylsulfonyl)indole**

To a solution of 1-(phenylsulfonyl)indole (500 mg, 1.94 mmol) in THF (5 ml) was added dropwise *tert*-butyllithium (1.4 ml, 2.33 mmol) under nitrogen atmosphere at -78 °C. The yellow solution was cannulated directly into a solution of *p*-chlorobenzoyl chloride (0.3 ml, 2.33 mmol) in THF (3 ml) cooled to -78 °C. The reaction mixture was stirred at -78 °C for 2 h. The mixture was quenched with saturated ammonium chloride and extracted with ethyl acetate (100 ml). The organic layer was washed with water (50 ml), brine (50 ml) and dried ( $\text{MgSO}_4$ ). After removal of solvent, the crude product was purified by flash column chromatography eluting with hexane/ethyl acetate (10:1) to afford 339 mg (44.1 %) of the title compound as yellow amorphous solids.

15       $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.13 (1H, d,  $J=8.4\text{Hz}$ ), 8.04-8.00 (2H, m), 7.93-7.90 (2H, m),  
15      7.58-7.44 (7H, m), 7.30 (1H, t,  $J=7.4\text{Hz}$ ), 6.95 (1H, s).

**STEP 2. 2-(4-Chlorobenzoyl)indole**

A mixture of 2-(4-chlorobenzoyl)-1-(phenylsulfonyl)indole (step 1, 334 mg, 0.84 mmol) and 2N sodium hydroxide (1.5 ml, 2.78 mmol) in ethanol (5 ml) was heated at reflux temperature for 15 min. The mixture was concentrated and the residue was diluted with ethyl acetate (100 ml). The organic layer was washed with water and dried ( $\text{MgSO}_4$ ), and concentrated to afford 211 mg (98.2 %) of the title compound as yellow solids.

25       $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 9.45 (1H, br.s), 7.97-7.92 (2H, m), 7.74-7.70 (1H, m), 7.54-7.47 (3H, m), 7.42-7.36 (1H, m), 7.21-7.13 (2H, m).

**STEP 3. Diethyl  $\alpha$ -acetoxymethyl-[2-(4-chlorobenzoyl)-1H-indol-3-yl]malonate**

The title compound was prepared according to the procedure described in step 4 of Example 2 (Method B) employing 2-(4-chlorobenzoyl)indole (step 2).

30       $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.94 (1H, br.s), 7.90 (1H, d,  $J=8.4\text{Hz}$ ), 7.81-7.77 (2H, m), 7.43-7.36 (3H, m), 7.32-7.26 (1H, m), 7.22-7.16 (1H, m), 4.27-4.14 (4H, m), 1.75 (3H, s),  
30      1.29-1.16 (6H, m).

STEP 4. Diethyl [2-(4-chlorobenzoyl)-1H-indol-3-yl]malonate

The title compound was prepared according to the procedure described in step 5 of Example 2 (Method B) employing diethyl  $\alpha$ -acetoxy-[2-(4-chlorobenzoyl)-1H-indol-3-yl]malonate (step 3).

5       $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.73 (1H, br.s), 7.85-7.82 (1H, m), 7.79-7.76 (2H, m), 7.52-7.46 (2H, m), 7.39-7.37 (1H, m), 7.26-7.19 (2H, m), 5.27 (1H, s), 4.26-4.16 (4H, m), 1.26-1.21 (6H, m)

STEP 5. [2-(4-Chlorobenzoyl)-1H-indol-3-yl]acetic acid

10     The title compound was prepared according to the procedure described in step 6 of Example 2 (Method B) employing diethyl [2-(4-chlorobenzoyl)-1H-indol-3-yl]malonate (step 4).

m.p.: 221-224 °C (recrystallized from ethyl acetate/hexane).

IR (KBr)  $\nu$ : 3321, 1697, 1607, 1576, 1529, 1433, 1408, 1339, 1263, 1223, 1202  $\text{cm}^{-1}$ .

15      $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$ : 11.62 (1H, s), 7.79-7.75 (2H, m), 7.71-7.63 (3H, m), 7.46 (1H, d,  $J=8.2\text{Hz}$ ), 7.35-7.29 (1H, m), 7.14-7.08 (1H, m), 3.84 (2H, s)

EXAMPLE 53[6-CHLORO-2-(2-FURYLCARBONYL)-1H-INDOL-3-YL]ACETIC ACIDSTEP 1. 6-chloro-2-(2-furylcarbonyl)-1-(phenylsulfonyl)indole

20     The title compound was prepared according the procedure decribed in step 1 of Example 2 (Method B) from 6-chloro-1-(phenylsulfonyl)indole (step 1 of Example 2 Method B) and 2-furoyl chloride.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.11-8.19 (3 H, m), 7.73-7.74 (1 H, m), 7.51-7.65 (4 H, m), 7.27-7.31 (2 H, m), 7.10 (1 H, s), 6.62-6.64 (1 H, m).

STEP 2. 6-Chloro-2-(2-furylcarbonyl)indole

25     The title compound was prepared according the procedure decribed in step 3 of Example 2 (Method B) from 6-chloro-2-(2-furylcarbonyl)-1-(phenylsulfonyl)indole (step 1).

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 9.33 (1 H, br s), 7.65-7.73 (3 H, m), 7.46-7.48 (2 H, m), 7.12-7.16 (1 H, m), 6.64-6.66 (1 H, m).

30     STEP 3. Diethyl  $\alpha$ -Acetoxy[6-chloro-2-(2-furylcarbonyl)indol-3-yl]malonate

The title compound was prepared according to the procedure decribed in step 4 of Example 2 (Method B) from 6-chloro-2-(2-furylcarbonyl)indole (step 2).

1 H-NMR (CDCl<sub>3</sub>) δ: 9.60 (1 H, br s), 7.76 (1 H, d, J=8.9 Hz), 7.62-7.63 (1 H, m), 7.43 (1 H, d, J=1.3 Hz), 7.28-7.29 (1 H, m), 7.13 (1 H, dd, J=1.8 Hz, 8.7 Hz), 6.59 (1 H, dd, J=1.6 Hz, 3.5 Hz), 4.18-4.32 (4 H, m), 1.88 (3 H, s), 1.18-1.28 (6 H, m).

STEP 4. Diethyl [6-chloro-2-(2-furylcarbonyl)indol-3-yl]malonate

The title compound was prepared according to the procedure decribed in step 5 of Example 2 (Method B) from diethyl α-acetoxy-[6-chloro-2-(2-furylcarbonyl)indol-3-yl]malonate (step 3).

10 1 H-NMR (CDCl<sub>3</sub>) δ: 9.83 (1 H, br s), 7.67 (1 H, t, J=0.8 Hz), 7.63 (1 H, d, J=8.9 Hz), 7.40 (1 H, d, J=3.6 Hz), 7.30 (1 H, d, J=1.8 Hz), 7.01 (1 H, dd, J=1.8 Hz, 8.9 Hz), 6.62 (1 H, dd, J=1.6 Hz, 2.1 Hz), 6.19 (1 H, s), 4.20-4.32 (4 H, m), 1.27 (6 H, t, J=7.3 Hz).

STEP 5. [6-Chloro-2-(2-furylcarbonyl)indol-3-yl]acetic acid.

The title compound was prepared according to the procedure decribed in step 15 6 of Example 2 (Method B) from diethyl [6-chloro-2-(2-furylcarbonyl)indol-3-yl]malonate (step 4).

1 H-NMR (DMSO-d<sub>6</sub>) δ: 12.22 (1 H, br s), 11.76 (1 H, br s), 8.13 (1 H, d, J=1.0 Hz), 7.75 (1 H, d, J=8.6 Hz), 7.56 (1 H, d, J=1.8 Hz), 7.48 (1 H, d, J=3.6 Hz), 7.14 (1 H, dd, J=1.8 Hz, 8.6 Hz), 6.85 (1 H, dd, J=1.8 Hz, 3.6 Hz), 4.02 (2 H, s).

20 **EXAMPLE 54**

[6-CHLORO-2-(CYCLOHEXANECARBONYL)-1H-INDOL-3-YL]ACETIC ACID

STEP 1. 6-chloro-2-cyclohexanecarbonyl-1-(phenylsulfonyl)indole

The title compound was prepared according to the procedure described in step 25 of Example 2 (Method B) from 6-chloro-1-(phenylsulfonyl)indole (step 1 of Example 2, Method B) and cyclohexanecarbonyl chloride.

tlc: R<sub>f</sub>=0.4 (ethyl acetate/hexane=1:4).

STEP 2. 6-Chloro-2-(cyclohexanecarbonyl)indole

The title compound was prepared according to the procedure described in step 30 of Example 2 (Method B) from 6-chloro-2-cyclohexanecarbonyl-1-(phenylsulfonyl)indole (step 1).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 10.08 (1H, br s), 8.08-7.04 (4H, m), 2.28-1.20(11H, m).

**STEP 3. Diethyl α-acetoxy-[6-chloro-2-(cyclohexanecarbonyl)-1H-indol-3-yl]malonate**

The title compound was prepared according to the procedure described in step 4 of Example 2 (Method B) from 6-chloro-2-(cyclohexanecarbonyl)indole (step 2).

5   <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.94 (1H, br s), 8.12-7.09 (3H, m), 4.34-4.21 (4H, m), 2.20 (3H, s), 1.81-1.20 (17H, m).

**STEP 4. Diethyl [6-chloro-2-(cyclohexanecarbonyl)-1H-indol-3-yl]malonate**

The title compound was prepared according to the procedure described in step 5 of Example 2 (Method B) from diethyl α-acetoxy-[6-chloro-2-(cyclohexanecarbonyl)-1H-indol-3-yl]malonate (step 3).

10   <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.90 (1H, br s), 7.72 (1H, d, J=8.72Hz), 7.36-7.09 (2H, m), 5.70 (1H, s), 4.28-4.19 (4H, m), 1.91-1.22 (17H, m).

**STEP 5. [6-Chloro-2-(cyclohexanecarbonyl)-1H-indol-3-yl]acetic acid**

The title compound was prepared according to the procedure described in step 6 of Example 2 (Method B) from diethyl [6-chloro-2-(cyclohexanecarbonyl)-1H-indol-3-yl] malonate (step 4).

m.p. : 206-209 °C

IR(KBr) ν : 3314, 2924, 2856, 1734, 1650, 1537, 1396, 1248, cm<sup>-1</sup>

15   <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.78 (1H, s), 7.71 (1H, d, J=8.64Hz), 7.46-7.07 (2H, m), 4.01 (2H, s), 1.78-1.16(11H).

**EXAMPLE 55**

**METHYL [6-CHLORO-2-(4-METHOXYBENZOYL)-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in Example 8 from methyl *trans*-4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of Example 8) and 4-methoxyphenacyl bromide.

20   <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.85 (1H, s), 7.82 (2H, d, J=8.9Hz), 7.56 (1H, d, J=8.6Hz), 7.40 (1H, d, J=1.8Hz), 7.15 (1H, dd, J=1.8, 8.6Hz), 6.99 (2H, d, J=8.6Hz), 3.90 (3H, s), 3.86 (2H, s), 3.67 (3H, s).

**EXAMPLE 56**

30   **[6-CHLORO-2-(4-METHOXYBENZOYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl [6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetate (step 1).

m.p.: 187-190 °C

- 5       $^1\text{H-NMR}$  (DMSO-d<sub>6</sub>) δ: 11.72 (1H, s), 7.78 (2H, d, J=8.7Hz), 7.70 (1H, d, J=8.6Hz), 7.49-7.45 (1H, m), 7.15-7.07 (3H, m), 3.87 (3H, s), 3.81 (2H, s).

**EXAMPLE 57**

**METHYL [6-CHLORO-2-(4-ETHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE**

10     A mixture of methyl *trans*-4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of Example 8, Method A, 700 mg, 1.99 mmol), 2-bromoacetyl-4-ethylpyridine\* (545 mg, 2.39 mmol), potassium carbonate (1.37 g, 13.9 mmol) and acetone (20 ml) was stirred at room temperature. After stirring for 3 h, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 0.6 ml, 3.98 mmol) was added. The resulting mixture was stirred for an additional 19 h and then concentrated. The residue was diluted with dichloromethane (200 ml) and washed with water (100 ml x 2). The organic layer was dried ( $\text{MgSO}_4$ ) and concentrated. The residue was purified by flash column chromatography eluting with ethyl acetate/hexane/dichloromethane (1:4:1) to give the title compound including impurity. The crude product was washed with ethyl acetate to give 297 mg (42%) of the title compound as yellow solids.

15       $^1\text{H-NMR}$  (CDCl<sub>3</sub>) δ: 12.52 (1H, br s), 8.64 (1H, d, J=4.9Hz), 8.21 (1H, br s), 7.62 (1H, d, J=8.7Hz), 7.52 (1H, d, J=1.8Hz), 7.39-7.35 (1H, m), 7.13 (1H, dd, J=1.8, 8.6Hz), 4.31 (2H, s), 3.73 (3H, s), 2.78 (2H, q, J=7.6Hz), 1.32 (3H, t, J=7.6Hz).

\* 2-Bromoacetyl-4-ethylpyridine was prepared as follows:

20     To a solution of 2-acetyl-4-ethylpyridine (E. C. Constable et al., *J. Am. Chem. Soc.*, 1997, 119, 5606., 8.37 g, 56.1 mmol) in 25% hydrobromic acid-acetic acid (150 ml) was added dropwise a solution of bromine (9.86 g, 61.7 mmol) in acetic acid (30 ml) with ice-cooling. The mixture was allowed to warm to room temperature and stirred for 2h. Diethyl ether (500 ml) was added to the mixture and the resulting mixture was cooled with an ice-bath. A brown oil, separated out from the solution, was collected by decantation. The oil was treated with saturated aqueous sodium

bicarbonate (50 ml) and extracted with diethyl ether (300 ml). The organic layer was dried ( $\text{MgSO}_4$ ) and concentrated to give 15.3 g (88%) of the title compound.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.56 (1H, d,  $J=5.1\text{Hz}$ ), 7.95 (1H, br s), 7.36-7.34 (1H, m), 4.86 (2H, s), 2.74 (2H, q,  $J=7.7\text{Hz}$ ), 1.29 (3H, t,  $J=7.6\text{Hz}$ ).

5    **EXAMPLE 58**

[6-CHLORO-2-(4-ETHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

A yellow suspension of methyl [6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 57, 297 mg, 0.83 mmol) in 2N aqueous sodium hydroxide (2.5 ml) and ethanol (20 ml) was heated at reflux temperature for 3 h. After cooling to room temperature, the mixture was neutralized with 2N aqueous hydrochloric acid (2.5 ml) and concentrated. The residue was diluted with THF (150 ml), dried ( $\text{MgSO}_4$ ) and concentrated. The residual solids were recrystallization from ethyl acetate to give 251 mg (88%) of the title compound as yellow solids.

15    MS (EI) m/z: 342 ( $\text{M}^+$ ).

m.p.: 215-216 °C (decomposition).

IR (KBr)  $\nu$ : 3206, 1707, 1643, 1595, 1535, 1421, 1227, 1192, 1140, 912, 777 cm<sup>-1</sup>.

$^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$ : 12.30 (1H, br s), 12.18 (1H, br s), 8.73 (1H, d,  $J=4.9\text{Hz}$ ), 7.98 (1H, br s), 7.79 (1H, d,  $J=8.7\text{Hz}$ ), 7.74 (1H, d,  $J=1.8\text{Hz}$ ), 7.62 (1H, br d,  $J=5.1\text{Hz}$ ), 7.12 (1H, dd,  $J=1.8$ , 8.6Hz), 4.08 (2H, s), 2.78 (2H, q,  $J=7.7\text{Hz}$ ), 1.26 (3H, t,  $J=7.7\text{Hz}$ ).

**EXAMPLE 59**

METHYL [5-CHLORO-2-(4-ETHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-chloro-2-(phenylsulfonylamino)cinnamate (Example 36, step 3) and 2-bromoacetyl-4-ethylpyridine (Preparation is described in Example 57).

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 12.57 (1H, br s), 8.65 (1H, d,  $J=5.1\text{Hz}$ ), 8.21 (1H, br s), 7.68 (1H, br s), 7.45 (1H, d,  $J=8.9\text{Hz}$ ), 7.40-7.36 (1H, m), 7.31 (1H, dd,  $J=2.0$ , 8.7Hz), 4.28 (2H, s), 3.74 (3H, s), 2.78 (2H, q,  $J=7.7\text{Hz}$ ), 1.32 (3H, t,  $J=7.7\text{Hz}$ ).

30    **EXAMPLE 60**

[5-CHLORO-2-(4-ETHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in Example 58 from methyl [5-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 59).

MS (EI) m/z: 342 ( $M^+$ ).

m.p.: 217-218 °C.

IR (KBr)  $\nu$ : 3269, 1705, 1643, 1595, 1533, 1418, 1335, 1225, 1200, 1059, 779 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 12.33 (1H, br s), 8.73 (1H, d, J=4.9Hz), 7.98 (1H, br s), 7.86 (1H, d, J=2.0Hz), 7.69 (1H, d, J=8.9Hz), 7.61 (1H, dd, J=4.8, 1.6Hz), 7.33 (1H, dd, J=2.0, 8.7Hz), 4.07 (2H, s), 2.78 (2H, q, J=7.6Hz), 1.26 (3H, t, J=7.6Hz).

**EXAMPLE 61**

METHYL [6-CHLORO-2-(4-ISOPROPYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and 2-bromoacetyl-4-isopropylpyridine\*.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 12.53 (1H, br s), 8.65 (1H, d, J=4.9Hz), 8.24 (1H, d, J=1.6Hz), 7.62 (1H, d, J=8.7Hz), 7.52 (1H, d, J=1.6Hz), 7.40 (1H, dd, J=1.8, 4.9Hz), 7.13 (1H, dd, J=1.8, 8.7Hz), 4.30 (2H, s), 3.73 (3H, s), 2.97-3.07 (1H, m), 1.32 (6H, d, J=6.9Hz).

\*2-Bromoacetyl-4-isopropylpyridine was prepared from 2-acetyl-4-isopropylpyridine (K.Ishihama et al., *J. Agric. Food Chem.*, 1992, **40**, 1647) according to the procedure for preparing 2-bromoacetyl-4-ethylpyridine described in Example 57.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 8.57 (1H, d, J=5.8Hz), 7.97-7.98 (1H, m), 7.36-7.38 (1H, m), 4.86 (2H, s), 2.94-3.04 (1H, m), 1.27-1.32 (6H, m).

**EXAMPLE 62**

[6-CHLORO-2-(4-ISOPROPYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in Example 58 from methyl [6-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 61).

m.p.: 194-196 °C.

IR (KBr) v: 3244, 2965, 1692, 1647, 1597, 1537, 1254, 1200, 1178, 1150, 764 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.28 (1H, br s), 8.74 (1H, d, J=5.3Hz), 8.01 (1H, s), 7.80 (1H, d, J=8.9Hz), 7.74 (1H, d, J=1.6Hz), 7.64-7.66 (1H, m), 7.12 (1H, dd, J=1.8, 8.6Hz).

5 4.08 (2H, s), 3.02-3.13 (1H, m), 1.28 (6H, d, J=6.9Hz).

#### EXAMPLE 63

##### METHYL [5-CHLORO-2-(4-ISOPROPYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in  
10 Example 57 from methyl *trans*-5-chloro-2-(penylsulfonylamino)cinnamate (Example 36, step 3) and 2-bromoacetyl-4-isopropylpyridine (Preparation is described in Example 61).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.57 (1H, br s), 8.65 (1H, d, J=5.1Hz), 8.24 (1H, d, J=1.6Hz),  
15 7.67 (1H, d, J=2.0Hz), 7.44 (1H, d, J=8.2Hz), 7.40 (1H, dd, J=1.8, 4.9Hz), 7.31 (1H, dd, J=2.0, 8.7Hz), 4.28 (2H, s), 3.74 (3H, s), 2.97-3.07 (1H, m), 1.32 (6H, d, J=6.9Hz).

#### EXAMPLE 64

##### [5-CHLORO-2-(4-ISOPROPYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in  
20 Example 58 from methyl [5-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 63).

MS (EI) m/z: 356 (M<sup>+</sup>).

m.p.: 227-228 °C.

IR (KBr) v: 2964, 1703, 1643, 1595, 1537, 1202, 1059, 768 cm<sup>-1</sup>.

25 <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.32 (1H, br s), 12.15 (1H, br s), 8.74 (1H, d, J=4.9Hz), 8.00 (1H, s), 7.86 (1H, s), 7.64-7.71 (2H, m), 7.31-7.35 (1H, m), 4.08 (2H, s), 3.03-3.13 (1H, m), 1.28 (6H, d, J=6.9Hz).

#### EXAMPLE 65

##### METHYL [6-CHLORO-2-(4-PROPYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE

30 YL]ACETATE

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-chloro-2-(penylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and 2-bromoacetyl-4-propylpyridine hydrobromide\*.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.53 (1H, br s), 8.64 (1H, d, J=4.9Hz), 8.19 (1H, s), 7.62 (1H, d, J=8.7Hz), 7.53 (1H, d, J=1.6Hz), 7.35-7.37 (1H, m), 7.13 (1H, dd, J=1.8, 8.7Hz), 4.31 (2H, s), 3.73 (3H, s), 2.71 (2H, t, J=7.3Hz), 1.69-1.77 (2H, m), 0.98 (3H, t, J=7.3Hz).

\*2-Bromoacetyl-4-propylpyridine hydrobromide was prepared as follows;

4-Propyl-2-pyridinecarbonitrile:

The title compound was prepared from 4-propylpyrinine-*N*-oxide (S.Gheretti et al., *J. Heterocycl. Chem.*, 1969, 6, 859) according to the procedure for preparing 4-chloro-2-pyridinecarbonitrile described in Example 33.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.59 (1H, d, J=5.1Hz), 7.53 (1H, s), 7.32-7.34 (1H, m), 2.66 (2H, t, J=7.3Hz), 1.62-1.76 (2H, m), 0.97 (3H, t, J=7.3Hz).

2-Acetyl-4-propylpyridine:

The title compound was prepared from 4-propyl-2-pyridinecarbonitrile according to the procedure for preparing 2-acetyl-4-chloropyridine described in Example 33.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.56 (1H, d, J=4.9Hz), 7.88 (1H, s), 7.27-7.30 (1H, m), 2.72 (3H, s), 2.66 (2H, t, J=7.4Hz), 1.62-1.76 (2H, m), 0.95 (3H, t, J=7.4Hz).

2-Bromoacetyl-4-propylpyridine hydrobromide:

The title compound was prepared from 2-acetyl-4-propylpyridine according to the procedure for preparing 2-bromoacetyl-4-methylpyridine hydrobromide described in step 2 of Example 31.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 8.64 (1H, d, J=4.9Hz), 7.90 (1H, d, J=1.0Hz), 7.59 (1H, dd, J=1.6, 4.9Hz), 5.02 (2H, s), 2.70 (2H, t, J=7.4Hz), 1.57-1.71 (2H, m), 0.89 (3H, t, J=7.3Hz).

#### **EXAMPLE 66**

**[6-CHLORO-2-(4-PROPYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 58 from methyl 2-[6-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 65).

m.p.: 189-191 °C.

- 5 IR (KBr) v: 2964, 2928, 1711, 1645, 1595, 1533, 1281, 1225, 1192, 799 cm<sup>-1</sup>.  
<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.28 (1H, br s), 8.73 (1H, d, J=5.1Hz), 7.96 (1H, s), 7.73-7.81 (2H, m), 7.59 (1H, d, J=4.9Hz), 7.10-7.13 (1H, m), 4.08 (2H, s), 2.73 (2H, t, J=7.1Hz), 1.63-1.72 (2H, m), 0.92 (3H, t, J=7.3Hz).

**EXAMPLE 67**

- 10 **METHYL [5-CHLORO-2-(4-PROPYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-chloro-2-(penylsulfonylamino)cinnamate (Example 36, step 3) and 2-bromoacetyl-4-propylpyridine hydrobromide (Preparation is described in Example 65).

- 15 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.56 (1H, br s), 8.64 (1H, d, J=4.9Hz), 8.18 (1H, s), 7.67 (1H, d, J=2.0Hz), 7.45 (1H, d, J=8.7Hz), 7.29-7.37 (2H, m), 4.28 (2H, s), 3.74 (3H, s), 2.73 (2H, t, J=7.4Hz), 1.80-1.66 (2H, m), 0.97 (3H, t, J=7.3Hz).

**EXAMPLE 68**

- 20 **[5-CHLORO-2-(4-PROPYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 58 from methyl [5-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 67).

- 25 m.p.: 208-209 °C.

- IR (KBr) v: 3296, 2957, 1705, 1645, 1595, 1535, 1329, 1273, 1204, 1057, 795 cm<sup>-1</sup>.  
<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.33 (1H, br s), 12.15 (1H, br s), 8.73 (1H, d, J=4.9Hz), 7.95 (1H, s), 7.86 (1H, s), 7.69 (1H, d, J=8.7Hz), 7.58-7.61 (1H, m), 7.31-7.35 (1H, m), 4.08 (2H, s), 2.73 (2H, t, J=7.4Hz), 1.64-1.72 (2H, m), 0.92 (3H, t, J=7.4Hz).

- 30 **EXAMPLE 69**

METHYL [2-(4-*tert*-BUTYLPYRIDINE-2-CARBONYL)-6-CHLORO-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-chloro-2-(penylsulfonylamino)cinnamate (step 1 of 5 Example 8, Method A) and 2-bromoacetyl-4-*tert*-butylpyridine\*.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.55 (1H, br s), 8.67 (1H, d, J=5.3Hz), 8.39 (1H, d, J=2.1Hz), 7.63 (1H, d, J=8.7Hz), 7.53-7.55 (2H, m), 7.13 (1H, dd, J=1.8, 8.7Hz), 4.31 (2H, s), 3.73 (3H, s), 1.38 (9H, s).

\*2-Bromoacetyl-4-*tert*-butylpyridine was prepared from 2-acetyl-4-*tert*-butylpyridine (E.C.Constable et al., *J. Am. Chem. Soc.*, 1997, 119, 5606) according to the procedure for preparing 2-bromoacetyl-4-ethylpyridine described in Example 57.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.58 (1H, d, J=4.8Hz), 8.11 (1H, d, J=1.6Hz), 7.51 (1H, dd, J=1.8, 5.1Hz), 4.86 (2H, s), 1.35 (9H, s).

**EXAMPLE 70**

15 [2-(4-*tert*-BUTYLPYRIDINE-2-CARBONYL)-6-CHLORO-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in Example 58 from methyl [2-(4-*tert*-butylpyridine-2-carbonyl)-6-chloro-1H-indol-3-yl]acetate (Example 69 ).

20 MS (EI) m/z: 370 (M<sup>+</sup>).

m.p.: 203-205 °C.

IR (KBr) ν: 2966, 1699, 1647, 1591, 1535, 1229 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.29 (1H, br s), 8.76 (1H, d, J=5.3Hz), 8.10 (1H, d, J=2.0Hz), 7.74-7.81 (3H, m), 7.12 (1H, dd, J=1.8, 8.6Hz), 4.08 (2H, s), 1.36 (9H, s).

25 **EXAMPLE 71**

METHYL [2-(4-*tert*-BUTYLPYRIDINE-2-CARBONYL)-5-CHLORO-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-chloro-2-(penylsulfonylamino)cinnamate (Example 30 36, step 3) and 2-bromoacetyl-4-*tert*-butylpyridine (Preparation is described in Example 69).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.59 (1H, br s), 8.67 (1H, d, J=5.3Hz), 8.38 (1H, d, J=2.0Hz), 7.68 (1H, d, J=2.0Hz), 7.54 (2H, dd, 2.0, 5.3Hz), 7.45 (1H, d, J=8.9Hz), 7.32 (1H, dd, J=2.0, 8.9Hz), 4.29 (2H, s), 3.74 (3H, s), 1.38 (9H, s).

**EXAMPLE 72**

- 5    [2-(4-*tert*-BUTYL PYRIDINE-2-CARBONYL)-5-CHLORO-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in Example 58 from methyl [2-(4-*tert*-butylpyridine-2-carbonyl)-5-chloro-1H-indol-3-yl]acetate (Example 71).

- 10    MS (EI) m/z: 370 (M<sup>+</sup>).

m.p.: 209-211 °C.

IR (KBr) ν: 3269, 2968, 1746, 1705, 1589, 1531, 1236, 1207, 1177, 1150, 1059, 737 cm<sup>-1</sup>.

- 15    <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.33 (1H, br s), 8.76 (1H, d, J=5.3Hz), 8.10 (1H, d, J=2.0Hz), 7.86 (1H, d, J=2.0Hz), 7.78 (1H, dd, J=2.0, 5.1Hz), 7.69 (1H, d, J=8.7Hz), 7.33 (1H, dd, J=2.0, 8.7Hz), 4.08 (2H, s), 1.36 (9H, s).

**EXAMPLE 73**

- METHYL [6-CHLORO-2-(3-METHYL PYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE

- 20    The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-chloro-2-(penylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and 2-bromoacetyl-3-methylpyridine hydrobromide\*.

- 25    <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 11.19 (1H, br s), 8.54 (1H, d, J=4.6Hz), 7.65 (1H, d, J=7.7Hz), 7.55 (1H, d, J=8.6Hz), 7.33-7.38 (2H, m), 7.06 (1H, dd, J=1.8, 8.7Hz), 4.15 (2H, s), 3.69 (3H, s), 2.59 (3H, s).

\*2-Bromoacetyl-3-methylpyridine hydrobromide was prepared from 2-acetyl-3-methylpyridine (T.A.Crabb et al., *Org. Magn. Reson.*, **1982**, 20, 242) according to the procedure for preparing 2-bromoacetyl-4-methylpyridine hydrobromide described in step 2 of Example 31.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 8.56 (1H, d, J=3.6Hz), 7.84 (1H, d, J=7.7Hz), 7.56-7.60 (1H, m), 5.01 (2H, s), 4.01 (3H, s).

**EXAMPLE 74**

**[6-CHLORO-2-(3-METHYL PYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC**

**5    ACID**

The title compound was prepared according to the procedure described in Example 58 from methyl [6-chloro-2-(3-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 73).

MS (EI) m/z: 328 (M<sup>+</sup>).

10    m.p.: 195-196 °C.

IR (KBr) v: 3314, 1703, 1636, 1526, 1418, 1396, 1231, 1196, 1150, 1109 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.14 (1H, br s), 11.76 (1H, br s), 8.53 (1H, d, J=3.8Hz), 7.85 (1H, d, J=7.9Hz), 7.74 (1H, d, J=8.6Hz), 7.52-7.56 (2H, m), 7.10 (1H, dd, J=1.8, 8.6Hz), 3.66 (2H, s), 2.33 (3H, s).

**15    EXAMPLE 75**

**METHYL [5-CHLORO-2-(3-METHYL PYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-chloro-2-(penylsulfonylamino)cinnamate (Example 36, step 3) and 2-bromoacetyl-3-methylpyridine hydrobromide (Preparation is described in Example 73).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 11.28 (1H, br s), 8.56 (1H, d, J=3.1Hz), 7.61-7.69 (2H, m), 7.23-7.41 (3H, m), 4.15 (2H, s), 3.70 (3H, s), 2.61 (3H, s).

**EXAMPLE 76**

**[5-CHLORO-2-(3-METHYL PYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC**

**ACID**

The title compound was prepared according to the procedure described in Example 58 from methyl [5-chloro-2-(3-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 75).

30    m.p.: 209-211°C (decomposed).

IR (KBr)  $\nu$ : 3379, 3271, 1728, 1649, 1638, 1528, 1231, 1195, 1182, 1165, 1015  $\text{cm}^{-1}$ .  
 $^1\text{H-NMR}$  (DMSO-d<sub>6</sub>)  $\delta$ : 11.81 (1H, br s), 8.53 (1H, d, J=4.4Hz), 7.85 (1H, d, J=7.7Hz),  
7.80 (1H, d, J=2.0Hz), 7.49-7.56 (2H, m), 7.31 (1H, dd, J=2.1, 8.7Hz), 3.66 (2H, s),  
2.33 (3H, s).

5 **EXAMPLE 77**

**METHYL [6-CHLORO-2-(6-METHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and 2-bromoacetyl-6-methylpyridine hydrobromide (H.Erlenmeyer, J.Jenni, and B.Prijs, *J.Med.Pharm.Chem.*, **1961**, 3, 561-566).

$^1\text{H-NMR}$  (CDCl<sub>3</sub>)  $\delta$ : 12.58 (1H, br s), 8.15 (1H, d, J=7.9Hz), 7.83 (1H, t, J=7.7Hz),  
7.62 (1H, d, J=8.7Hz), 7.51 (1H, d, J=1.8Hz), 7.40 (1H, d, J=7.7Hz), 7.13 (1H, dd,  
J=1.8, 8.7Hz), 4.31 (2H, s), 3.72 (3H, s), 2.76 (3H, s).

15 **EXAMPLE 78**

**[6-CHLORO-2-(6-METHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 58 from methyl [6-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 77).

MS (EI) m/z: 328 (M<sup>+</sup>).

m.p.: 230-231°C.

IR (KBr)  $\nu$ : 3273, 1697, 1643, 1535, 1308, 1227, 1183, 1150, 797, 760, 671  $\text{cm}^{-1}$ .

$^1\text{H-NMR}$  (DMSO-d<sub>6</sub>)  $\delta$ : 12.06 (1H, br s), 7.99 (1H, t, J=7.7Hz), 7.87 (1H, d, J=7.6Hz),  
7.78 (1H, d, J=8.9Hz), 7.74 (1H, d, J=2.0Hz), 7.59 (1H, d, J=7.6Hz), 7.13 (1H, dd,  
J=2.0, 8.7Hz), 4.04 (2H, s), 2.69 (3H, s).

**EXAMPLE 79**

**METHYL [5-CHLORO-2-(5-METHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE**

30 The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-chloro-2-(phenylsulfonylamino)cinnamate (Example

36, step 3) and 2-bromoacetyl-5-methylpyridine (Preparation is described in step 1 of Example 32).

5       <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.48 (1H, br s), 8.59 (1H, d, J=2.1Hz), 8.24 (1H, d, J=8.1Hz), 7.75 (1H, dd, J=2.1, 8.1Hz), 7.67 (1H, d, J=2.0Hz), 7.44 (1H, d, J=8.7Hz), 7.31 (1H, dd, J=2.0, 8.9Hz), 4.29 (2H, s), 3.74 (3H, s), 2.48 (3H, s).

**EXAMPLE 80**

**[5-CHLORO-2-(5-METHYL PYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in 10 Example 58 from methyl [5-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 79).

MS (EI) m/z: 328 (M<sup>+</sup>).

m.p.: 247-248 °C.

IR (KBr) ν: 3288, 1699, 1638, 1531, 1427, 1329, 1285, 1246, 1209, 1177, 1059, 1016, 15 800, 700 cm<sup>-1</sup>.

1       <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.30 (1H, br s), 12.15 (1H, br s), 8.68 (1H, br s), 8.04 (1H, d, J=7.9Hz), 7.93 (1H, br d, J=8.9Hz), 7.84 (1H, br s), 7.69 (1H, d, J=8.9Hz), 7.33 (1H, dd, J=2.0, 8.9Hz), 4.09 (2H, s), 2.46 (3H, s).

**EXAMPLE 81**

20       **METHYL [6-CHLORO-2-[5-(TRIFLUOROMETHYL)PYRIDINE-2-CARBONYL]-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and 2-bromoacetyl-5-(trifluoromethyl)pyridine\*.

25       <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 11.97 (1H, br s), 9.07 (1H, br s), 8.48 (1H, d, J=8.4Hz), 8.23 (1H, dd, J=2.1, 8.4Hz), 7.63 (1H, d, J=8.6Hz), 7.52 (1H, d, J=1.8Hz), 7.15 (1H, dd, J=1.8, 8.6Hz), 4.31 (2H, s), 3.74 (3H, s).

\* 2-Bromoacetyl-5-(trifluoromethyl)pyridine was prepared from 2-chloro-5-(trifluoromethyl)pyridine according to the procedure for preparing 2-bromoacetyl-5-methylpyridine described in step 1 of Example 32.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.96 (1H, br s), 8.23 (1H, br d, J=8.2Hz), 8.13 (1H, dd, J=2.1, 8.1Hz), 4.83 (2H, s).

**EXAMPLE 82**

**[6-CHLORO-2-[5-(TRIFLUOROMETHYL)PYRIDINE-2-CARBONYL]-1H-INDOL-**

**5   3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 58 from methyl [6-chloro-2-(5-trifluoromethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 81).

MS (EI) m/z: 382 (M<sup>+</sup>).

10   m.p.: 228-229°C.

IR (KBr) ν: 3325, 1707, 1636, 1529, 1333, 1310, 1138, 1078, 1020 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.05 (1H, br s), 9.17 (1H, br s), 8.54 (1H, dd, J=2.0, 8.4Hz), 8.24 (1H, d, J=8.2Hz), 7.82 (1H, d, J=8.6Hz), 7.64 (1H, d, J=1.8Hz), 7.14 (1H, dd, J=2.0, 8.7Hz), 4.06 (2H, s).

15   **EXAMPLE 83**

**METHYL [5-CHLORO-2-[5-(TRIFLUOROMETHYL)PYRIDINE-2-CARBONYL]-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-chloro-2-(phenylsulfonylamino)cinnamate (Example 20 36, step 3) and 2-bromoacetyl-5-(trifluoromethyl)pyridine (Preparation is described in Example 81).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.01 (1H, br s), 9.05 (1H, br s), 8.45 (1H, d, J=8.2Hz), 8.21 (1H, dd, J=2.3, 8.4Hz), 7.65 (1H, br s), 7.43 (1H, d, J=8.7Hz), 7.32 (1H, dd, J=2.0, 8.7Hz), 4.27 (2H, s), 3.76 (3H, s).

25   **EXAMPLE 84**

**[5-CHLORO-2-[5-(TRIFLUOROMETHYL)PYRIDINE-2-CARBONYL]-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 58 from methyl [5-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate (Example 83).

MS (EI) m/z: 382 ( $M^+$ ).

m.p.: 230-231°C.

IR (KBr)  $\nu$ : 3300, 1720, 1701, 1641, 1531, 1327, 1235, 1163, 1130, 1078, 1020, 864 cm<sup>-1</sup>.

- 5     <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 12.09 (1H, br s), 9.17 (1H, br s), 8.54 (1H, dd, J=2.0, 8.2Hz), 8.23 (1H, d, J=8.2Hz), 7.89 (1H, d, J=1.8Hz), 7.62 (1H, d, J=8.9Hz), 7.36 (1H, dd, J=1.8, 8.9Hz), 4.06 (2H, s).

**EXAMPLE 85**

- 10    METHYL [5-CHLORO-2-(5-CHLOROPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-chloro-2-(phenylsulfonylamino)cinnamate (Example 36, step 3) and 2-bromoacetyl-5-chloropyridine \*.

- 15    <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 12.01 (1H, br s), 8.72 (1H, d, J=2.5Hz), 8.29 (1H, d, J=8.6Hz), 7.93 (1H, dd, J=2.5, 8.6Hz), 7.65 (1H, d, J=2.0Hz), 7.43 (1H, d, J=8.7Hz), 7.31 (1H, dd, J=2.0, 8.7Hz), 4.27 (2H, s), 3.75 (3H, s).

\* 2-Bromoacetyl-5-chloropyridine was prepared from 2-bromo-5-chloropyridine (J. *Am. Chem. Soc.*, 1946, 68, 2574) according to the procedure for preparing 2-bromoacetyl-5-methylpyridine described in step 1 of Example 32.

- 20    <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 8.63 (1H, dd, J=0.6, 2.5Hz), 8.06 (1H, dd, J=0.6, 8.4Hz), 7.88 (1H, dd, J=2.3, 8.4Hz), 4.79 (2H, s).

**EXAMPLE 86**

[5-CHLORO-2-(5-CHLOROPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

- 25    The title compound was prepared according to the procedure described in Example 58 from methyl [5-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 85).

MS (EI) m/z: 348 ( $M^+$ ).

m.p.: 259-260 °C.

- 30    IR (KBr)  $\nu$ : 3314, 1703, 1632, 1528, 1331, 1236, 1178, 1111, 1059, 1015, 806, 698 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.18 (1H, br s), 12.08 (1H, br s), 8.84 (1H, d, J=2.5Hz), 8.25 (1H, dd, J=2.5, 8.4Hz), 8.10 (1H, d, J=8.6Hz), 7.87 (1H, d, J=2.0Hz), 7.63 (1H, d, J=8.7Hz), 7.34 (1H, dd, J=2.1, 8.9Hz), 4.06 (2H, s).

**EXAMPLE 87**

- 5    **METHYL [6-CHLORO-2-(5-CHLOROPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and 2-bromoacetyl-5-chloropyridine (Preparation is described 10 in Example 85).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 11.98 (1H, br s), 8.74 (1H, dd, J=0.7 and 2.3Hz), 8.31 (1H, dd, J=0.7, 8.6Hz), 7.94 (1H, dd, J=2.3, 8.4Hz), 7.63 (1H, d, J=8.7Hz), 7.52 (1H, d, J=1.6Hz), 7.14 (1H, dd, J=1.8, 8.7Hz), 4.30 (2H, s), 3.73 (3H, s).

**EXAMPLE 88**

- 15    **[6-CHLORO-2-(5-CHLOROPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 58 from methyl [6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 87).

- 20    MS (EI) m/z: 348 (M<sup>+</sup>).

m.p.: 242-244 °C.

IR (KBr) v: 3306, 1703, 1636, 1529, 1308, 1234, 1151, 1109, 698 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.05 (1H, br s), 8.84 (1H, d, J=2.3Hz), 8.26 (1H, dd, J=2.3, 8.4Hz), 8.10 (1H, d, J=8.4Hz), 7.80 (1H, d, J=8.7Hz), 7.67 (1H, d, J=1.8Hz), 7.13 (1H, dd, J=1.8, 8.7Hz), 4.06 (2H, s).

**EXAMPLE 89**

- METHYL [5-CHLORO-2-(4-CHLOROPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in 30 Example 57 from methyl *trans*-5-chloro-2-(phenylsulfonylamino)cinnamate (Example

36, step 3) and 2-bromoacetyl-4-chloropyridine hydrobromide (Preparation is described in Example 33).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.20 (1H, br s), 8.67 (1H, d, J=5.3Hz), 8.33 (1H, d, J=2.1Hz), 7.66 (1H, d, J=2.0Hz), 7.56 (1H, dd, J=2.1, 5.3Hz), 7.43 (1H, d, J=8.7Hz), 7.32 (1H, dd, J=2.0, 8.9Hz), 4.27 (2H, s), 3.75 (3H, s).

#### EXAMPLE 90

##### [5-CHLORO-2-(4-CHLOROPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in Example 58 from methyl [5-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 89).

MS (EI) m/z: 348 (M<sup>+</sup>).

m.p.: 243-244 °C.

IR (KBr) ν: 3000, 1719, 1643, 1528, 1242, 1202, 741 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.20 (1H, br s), 8.80 (1H, d, J=5.3Hz), 8.12 (1H, d, J=2.1Hz), 7.90 (1H, dd, J=2.1, 5.4Hz), 7.66 (1H, d, J=8.9Hz), 7.34 (1H, dd, J=2.0, 8.7Hz), 4.06 (2H, s).

#### EXAMPLE 91

##### METHYL [6-CHLORO-2-(PYRIDINE-3-CARBONYL)-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and 3-bromoacetylpyridine hydrobromide (G. B. Barlin, L. P. Davies, S. J. Ireland, M. M. L. Ngu, *Aust. J. Chem.*, 1989, **42**, 1735).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.26 (1H, br s), 9.00 (1H, dd, J=0.8, 2.1Hz), 8.80 (1H, dd, J=1.6, 4.8Hz), 8.10 (1H, dt, J=2.0, 2.0, 7.9Hz), 7.58 (1H, d, J=8.7Hz), 7.47 (1H, ddd, J=0.8, 4.9, 7.9Hz), 7.37 (1H, d, J=1.8Hz), 7.16 (1H, dd, J=1.8, 8.6Hz), 3.84 (2H, s), 3.65 (3H, s).

#### EXAMPLE 92

##### [6-CHLORO-2-(PYRIDINE-3-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in Example 58 from methyl [6-chloro-2-(pyridine-3-carbonyl)-1H-indol-3-yl]acetate (Example 91).

MS (EI) m/z: 314 ( $M^+$ ).

5 m.p.: 267-268 °C.

IR (KBr)  $\nu$ : 3346, 1705, 1609, 1566, 1528, 1433, 1418, 1327, 1267, 1215, 943, 761 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 12.28 (1H, br s), 11.86 (1H, br s), 8.90 (1H, br s), 8.85 (1H, br d, J=4.9Hz), 8.12 (1H, dt, J=2.0, 2.0, 7.9Hz), 7.77 (1H, t, J=8.6Hz), 7.62 (1H, dd, J=4.9, 8.0Hz), 7.49 (1H, d, J=2.0Hz), 7.15 (1H, dd, J=1.6, 8.4Hz), 3.85 (2H, s).  
10

### EXAMPLE 93

#### METHYL [6-CHLORO-2-(PYRIDINE-4-CARBONYL)-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in  
15 Example 57 from methyl *trans*-4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and 4-bromoacetylpyridine hydrobromide (L. W. Deady, M. S. Stanborough, *Aust. J. Chem.*, **1981**, 34, 1295).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 9.21 (1H, br s), 8.82-8.79 (2H, m), 7.59-7.57 (2H, m), 7.56 (1H, d, J=8.7Hz), 7.33 (1H, d, J=1.8Hz), 7.16 (1H, dd, J=1.8, 8.7Hz), 3.80 (2H, s), 3.65 (3H, s).  
20

### EXAMPLE 94

#### [6-CHLORO-2-(PYRIDINE-4-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in Example 58 from methyl [6-chloro-2-(pyridine-4-carbonyl)-1H-indol-3-yl]acetate  
25 (Example 93).

MS (EI) m/z: 314 ( $M^+$ ).

m.p.: 256-257 °C.

IR (KBr)  $\nu$ : 3352, 1709, 1607, 1528, 1431, 1329, 1259, 1202, 772, 687 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 11.82 (1H, br s), 8.82 (2H, d, J=5.8Hz), 7.77 (1H, d, J=8.6Hz),  
30 7.64-7.62 (2H, m), 7.48 (1H, d, J=1.8Hz), 7.15 (1H, dd, J=2.0, 8.7Hz), 3.83 (2H, s).

**EXAMPLE 95****METHYL [6-CHLORO-2-[4-(HYDROXYMETHYL)PYRIDINE-2-CARBONYL]-1H-INDOL-3-YL]ACETATE**

5 **STEP 1.** Methyl [6-chloro-2-[4-(*tert*-butyldimethylsilyloxy)methyl]pyridine-2-carbonyl]-1H-indol-3-yl]acetate

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-chloro-2-(penylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and 2-bromoacetyl-4-(*tert*-butyldimethylsilyloxy)methyl)pyridine\*.

10 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.47 (1H, br s), 8.70 (1H, d, J=4.9Hz), 8.21-8.22 (1H, m), 7.55-7.58 (2H, m), 7.50-7.51 (1H, m), 7.10 (1H, dd, J=1.8, 8.7Hz), 4.83 (2H, s), 4.31 (2H,s), 3.72 (3H, s), 0.98 (9H, s), 0.15 (6H, s).

2-Bromoacetyl-4-(*tert*-butyldimethylsilyloxy)methyl)pyridine was prepared as follows.  
2-Acetyl-4-(*tert*-butyldimethylsilyloxy)methyl)pyridine:

15 The title compound was prepared from 4-(*tert*-butyldimethylsilyloxy)methyl)pyridinecarbonitrile (A.Hadri et al., *J. Heterocycl. Chem.*, 1993, 30, 631) according to the procedure for preparing 2-acetyl-4-chloropyridine described in Example 33.

10 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.64 (1H, d, J=4.8Hz), 7.96 (1H, s), 7.50 (1H, d, J=4.8Hz), 4.83 (2H, s), 2.73 (3H, s), 0.96 (9H, s), 0.12 (6H, s).

2-Bromoacetyl-4-(*tert*-butyldimethylsilyloxy)methyl)pyridine:

To a solution of 2-acetyl-4-(*tert*-butyldimethylsilyloxy)methyl)pyridine (1.84 g, 6.932 mmol) in THF (50 ml) was added dropwise a solution of lithium bis(trimethylsilyl)amide (1M in THF, 8.3 ml, 8.3 mmol) at -78 °C. After stirring for 1h, chlorotriethylsilane (1.7 ml, 10.4 mmol) was added to the mixture at -78 °C. The mixture was stirred at the same temperature for 1h, then allowed to warm to 0 °C. After stirring for 1h, saturated aqueous ammonium chloride (50 ml) was added. The mixture was extracted with diethyl ether (100 ml). The organic layer was washed with water (50 ml), dried (MgSO<sub>4</sub>) and concentrated. The residue was dissolved in THF (20 ml), and then water (4 ml) and NBS were added at 0 °C. After stirring for 1h, the mixture was diluted with diethyl ether (200 ml), washed with water (50 ml) and

dried ( $MgSO_4$ ). Removal of solvent gave the crude product. Purification by flash column chromatography eluting with ethyl acetate/hexane (1:20) to afford 0.74 g (31%) of the title compound as crystals.

- 5       $^1H$ -NMR ( $CDCl_3$ )  $\delta$ : 8.63 (1H, d,  $J=4.8Hz$ ), 8.02 (1H, q,  $J=0.8Hz$ ), 7.53 (1H, dt,  $J=0.8, 4.9Hz$ ), 4.87 (2H, s), 4.81 (2H, s), 0.96 (9H, s), 0.13 (3H, s).

STEP 2. Methyl [6-chloro-2-[4-(hydroxymethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate

To a solution of methyl [6-chloro-2-[4-(*tert*-butyldimethylsilyloxy)methyl]pyridine-2-carbonyl]-1H-indol-3-yl]acetate (step 1, 10 171.5 mg, 0.3625 mmol) in THF (5 ml) was added a solution of tetrabutylammonium fluoride (1M in THF, 0.54 ml, 0.54 mmol) at room temperature. After stirring for 1h, the mixture was concentrated. The residue was diluted with ethyl acetate (100 ml), washed with water (20 ml x 2) and dried ( $MgSO_4$ ). Removal of solvent gave the crude product. Purification by flash column chromatography eluting with ethyl 15 acetate/hexane/dichloromethane (1:1:1) to afford 69.6 mg (54%) of the title compound as crystals.

- 17       $^1H$ -NMR ( $CDCl_3$ )  $\delta$ : 12.43 (1H, br s), 8.74 (1H, d,  $J=5.1Hz$ ), 8.29 (1H, s), 7.59-7.64 (2H, m), 7.52 (1H, d,  $J=1.5Hz$ ), 7.13 (1H, dd,  $J=1.6, 8.6Hz$ ), 4.86 (2H, d,  $J=5.1Hz$ ), 4.31 (2H, s), 3.73 (3H, s).

20      **EXAMPLE 96**

[6-CHLORO-2-[4-(HYDROXYMETHYL)PYRIDINE-2-CARBONYL]-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in Example 58 from methyl [6-chloro-2-[4-(hydroxymethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate (Example 95).

MS (EI) m/z: 344 ( $M^+$ ).

m.p.: 210-212 °C.

IR (KBr)  $\nu$ : 3304, 1728, 1713, 1622, 1583, 1526, 1194  $cm^{-1}$ .

- 30       $^1H$ -NMR ( $DMSO-d_6$ )  $\delta$ : 12.31 (1H, br s), 8.78 (1H, d,  $J=4.8Hz$ ), 8.08 (1H, s), 7.80 (1H, d,  $J=8.6Hz$ ), 7.74 (1H, d,  $J=1.8Hz$ ), 7.67 (1H, d,  $J=4.9Hz$ ), 7.12 (1H, dd,  $J=1.8, 8.7Hz$ ), 4.69 (2H, s), 4.09 (2H, s).

**EXAMPLE 97**

METHYL [5-CHLORO-2-[4-(HYDROXYMETHYL)PYRIDINE-2-CARBONYL]-1H-INDOL-3-YL]ACETATE

5      STEP 1. Methyl [5-chloro-2-[4-(*tert*-butyldimethylsilyloxy)methyl]pyridine-2-carbonyl]-1H-indol-3-yl]acetate

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-chloro-2-(penylsulfonylamino)cinnamate (Example 36, step 3) and 2-bromoacetyl-4-(*tert*-butyldimethylsilyloxy)methyl)pyridine (Preparation is described in step 1 of Example 95).

10      $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 12.47 (1H, br s), 8.66 (1H, d,  $J=4.9\text{Hz}$ ), 8.18 (1H, s), 7.60-7.61 (1H, m), 7.54-7.57 (1H, m), 7.39 (1H, d,  $J=8.9\text{Hz}$ ), 7.25 (1H, dd,  $J=2.0, 8.9\text{Hz}$ ), 4.82 (2H, s), 4.27 (2H, s), 3.74 (3H, s), 0.98 (9H, s), 0.14 (6H, s).

15     STEP 2. Methyl [5-chloro-2-[4-(hydroxymethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate

15     The title compound was prepared according to the procedure described in step 2 of Example 95 from methyl [5-chloro-2-[4-(*tert*-butyldimethylsilyloxy)methyl]pyridine-2-carbonyl]-1H-indol-3-yl]acetate (step 1).

20      $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 12.48 (1H, br s), 8.75 (1H, d,  $J=4.9\text{Hz}$ ), 8.31 (1H, s), 7.68 (1H, s), 7.60-7.62 (1H, m), 7.45 (1H, d,  $J=8.91\text{Hz}$ ), 7.32 (1H, dd,  $J=2.0, 8.9\text{Hz}$ ), 4.87 (2H, d,  $J=5.4\text{Hz}$ ), 4.28 (2H, s), 3.74 (3H, s).

**EXAMPLE 98**

[5-CHLORO-2-[4-(HYDROXYMETHYL)PYRIDINE-2-CARBONYL]-1H-INDOL-3-YL]ACETIC ACID

25     The title compound was prepared according to the procedure described in Example 58 from methyl [5-chloro-2-[4-(hydroxymethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate (Example 97).

MS (EI)  $m/z$ : 344 ( $\text{M}^+$ ).

m.p.: 218-219 °C.

IR (KBr)  $\nu$ : 3263, 1705, 1641, 1595, 1528, 1327, 1198, 1061  $\text{cm}^{-1}$ .

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.34 (1H, br s), 8.77 (1H, d, J=4.9Hz), 8.08 (1H, s), 7.85 (1H, s), 7.66-7.71 (2H, m), 7.33 (1H, dd, J=1.8, 8.9Hz), 5.63 (1H, br s), 4.68 (2H, s), 4.09 (2H, s).

#### EXAMPLE 99

- 5 METHYL [5-CHLORO-2-(3,4-DIMETHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-chloro-2-(phenylsulfonylamino)cinnamate (Example 36, step 3) and 2-bromoacetyl-3,4-dimethylpyridine hydrobromide\*.

- 10 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.20 (1H, br s), 8.67 (1H, d, J=5.3Hz), 8.33 (1H, d, J=2.1Hz), 7.66 (1H, d, J=2.0Hz), 7.56 (1H, dd, J=2.1, 5.3Hz), 7.43 (1H, d, J=8.7Hz), 7.32 (1H, dd, J=2.0, 8.9Hz), 4.27 (2H, s), 3.75 (3H, s).

\* 2-Bromoacetyl-3,4-dimethylpyridine hydrobromide was prepared as follows:  
3,4-Dimethylpyridine-2-carbonitrile:

- 15 The title compound including 4,5-dimethylpyridine-2-carbonitrile in the ratio of 5.5 to 1 was prepared from 3,4-dimethylpyridine-*N*-oxide (Abramovitch et al., *J. Org. Chem.*, 1972, 37, 1690) according to the procedure for preparing 4-chloro-2-pyridinecarbonitrile described in Example 33.

2-Acetyl-3,4-dimethylpyridine:

- 20 The title compound was prepared along with 2-acetyl-4,5-dimethylpyridine from 3,4-dimethylpyridine-2-carbonitrile including 4,5-dimethylpyridine-2-carbonitrile in the ratio of 5.5 to 1 according to the procedure for preparing 2-acetyl-4-chloropyridine described in Example 33.

2-acetyl-3,4-dimethylpyridine: <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.34 (1H, d, J=4.6Hz), 7.19 (1H, d, J=4.8Hz), 2.69 (3H, s), 2.43 (3H, s), 2.34 (3H, s).

2-acetyl-4,5-dimethylpyridine: <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.39 (1H, s), 7.83 (1H, s), 2.70 (3H, s), 2.33 (3H, s), 2.32 (3H, s).

2-Bromoacetyl-3,4-dimethylpyridine hydrobromide:

- 30 The title compound was prepared from 2-acetyl-3,4-dimethylpyridine according to the method of H. McKennis, Jr., L.B.Turnbull, E.R.Bowman, and E.Tamaki (in *J.Org.Chem.*, 1963, 23, 383-387).

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 8.39 (1H, d, J=4.8Hz), 7.46 (1H, d, J=4.8Hz), 4.96 (2H, s), 2.38 (3H, s), 2.35 (3H, s).

**EXAMPLE 100**

**[5-CHLORO-2-(3,4-DIMETHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 58 from methyl [5-chloro-2-(3,4-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 99).

MS (EI) m/z: 342 (M<sup>+</sup>).

10 m.p.: 236-237 °C.

IR (KBr) ν: 3395, 1710, 1641, 1526, 1339, 1281, 1196, 1053, 1007 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.76 (1H, br s), 8.37 (1H, d, J=4.9Hz), 7.79 (1H, d, J=2.0Hz), 7.48 (1H, d, J=8.7Hz), 7.41 (1H, d, J=4.9Hz), 7.31 (1H, dd, J=2.0, 8.7Hz), 3.56 (2H, s), 2.35 (3H, s), 2.16 (3H, s).

15 **EXAMPLE 101**

**METHYL [5-CHLORO-2-(4,5-DIMETHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-chloro-2-(phenylsulfonylamino)cinnamate (Example 20 36, step 3) and 2-bromoacetyl-4,5-dimethylpyridine\*.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.59 (1H, br s), 8.47 (1H, s), 8.12 (1H, s), 7.67 (1H, d, J=1.8Hz), 7.44 (1H, d, J=9.4Hz), 7.30 (1H, dd, J=2.0, 8.7Hz), 4.28 (2H, s), 3.73 (3H, s), 2.38 (6H, s).

\* 2-Bromoacetyl-3,4-dimethylpyridine was prepared from 2-acetyl-4,5-dimethylpyridine (Preparation is described in Example 99) according to the procedure for preparing 2-bromoacetyl-4-ethylpyridine described in Example 57.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.39 (1H, s), 7.87 (1H, s), 4.83 (2H, s), 2.35 (3H, s), 2.34 (3H, s).

**EXAMPLE 102**

**[5-CHLORO-2-(4,5-DIMETHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-**

30 **YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 58 from methyl [5-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 101).

MS (EI) m/z: 342 ( $M^+$ ).

5 m.p.: 245-246 °C.

IR (KBr)  $\nu$ : 3281, 1697, 1638, 1589, 1535, 1254, 1232, 1188, 1060, 802 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 12.34 (1H, br s), 12.15 (1H, br s), 8.57 (1H, s), 7.93 (1H, s), 7.84 (1H, d, J=1.8Hz), 7.69 (1H, d, J=8.7Hz), 7.32 (1H, dd, J=2.0, 8.7Hz), 4.09 (2H, s), 2.39 (3H, s), 2.38 (3H, s).

10 **EXAMPLE 103**

**METHYL [6-CHLORO-2-(4,5-DIMETHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and 2-bromoacetyl-4,5-dimethylpyridine (Preparation is described in Example 99).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 12.55 (1H, br s), 8.47 (1H, s), 8.12 (1H, s), 7.62 (1H, d, J=8.6Hz), 7.52 (1H, d, J=1.8Hz), 7.13 (1H, dd, J=1.8, 8.6Hz), 4.31 (2H, s), 3.72 (3H, s), 2.39 (6H, s).

20 **EXAMPLE 104**

**[6-CHLORO-2-(4,5-DIMETHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 58 from methyl [6-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 103).

MS (EI) m/z: 342 ( $M^+$ ).

m.p.: 226-228 °C.

IR (KBr)  $\nu$ : 3275, 1697, 1638, 1537, 1258, 1188, 799 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 12.30 (1H, br s), 8.57 (1H, s), 7.94 (1H, s), 7.78 (1H, d, J=8.7Hz), 7.74 (1H, d, J=1.8Hz), 7.11 (1H, dd, J=2.0, 8.6Hz), 4.09 (2H, s), 2.39 (3H, s), 2.38 (3H, s).

**EXAMPLE 105****METHYL [6-CHLORO-2-(4-METHOXYPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in  
5 Example 57 from methyl *trans*-4-chloro-2-(penylsulfonylamino)cinnamate (step 1 of  
Example 8, Method A) and 2-bromoacetyl-4-methoxypyridine hydrobromide\*.

- <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.61 (1H, br s), 8.57 (1H, d, J=5.9Hz), 7.89 (1H, d, J=2.6Hz),  
7.63 (1H, d, J=8.6Hz), 7.52 (1H, d, J=1.8Hz), 7.13 (1H, dd, J=1.8, 8.7Hz), 7.04 (1H,  
dd, J=2.6, 5.8Hz), 4.30 (2H, s), 3.96 (3H, s), 3.73 (3H, s).
- 10 \*2-Bromoacetyl-4-methoxypyridine hydrobromide was prepared from 2-acetyl-4-methoxypyridine (B. Case et al., *J. Org. Chem.*, 1961, 26, 4415) according to the procedure for preparing 2-bromoacetyl-4-methylpyridine hydrobromide described in step 2 of Example 31.
- <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 8.59-8.62 (1H, m), 7.63-7.65 (1H, m), 7.33-7.37 (1H, m), 5.63  
15 (2H, s), 3.96 (3H, s).

**EXAMPLE 106****[6-CHLORO-2-(4-METHOXYPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in  
20 Example 58 from methyl [6-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 105).

- MS (EI) m/z: 344 (M<sup>+</sup>).  
m.p.: 213 °C (decomposed).  
IR (KBr) ν: 3200, 1709, 1645, 1589, 1533, 1225, 1207 cm<sup>-1</sup>.
- 25 <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.35 (1H, br s), 12.18 (1H, br s), 8.66 (1H, d, J=5.6Hz), 7.80  
(1H, d, J=8.9Hz), 7.74 (1H, d, J=1.8Hz), 7.63 (1H, d, J=2.6Hz), 7.31 (1H, dd, J=2.9,  
5.1Hz), 7.12 (1H, dd, J=1.3, 8.7Hz), 4.09 (2H, s), 3.96 (3H, s).

**EXAMPLE 107****METHYL [5-CHLORO-2-(4-METHOXYPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-chloro-2-(penylsulfonylamino)cinnamate (Example 36, step 3) and 2-bromoacetyl-4-methoxypyridine hydrobromide (Preparation is described in Example 105).

- 5       $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 12.65 (1H, br s), 8.57 (1H, d,  $J=5.8\text{Hz}$ ), 7.88 (1H, d,  $J=2.5\text{Hz}$ ), 7.68 (1H, d,  $J=2.0\text{Hz}$ ), 7.45 (1H, dd,  $J=0.5, 8.7\text{Hz}$ ), 7.32 (1H, dd,  $J=1.8, 8.7\text{Hz}$ ), 7.05 (1H, dd,  $J=2.8, 5.8\text{Hz}$ ), 4.28 (2H, s), 3.96 (3H, s), 3.74 (3H, s).

**EXAMPLE 108**

- [5-CHLORO-2-(4-METHOXYPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 58 from methyl [5-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 107).

m.p.: 228°C (decomposed).

- 15     IR (KBr)  $\nu$ : 3230, 1707, 1647, 1595, 1566, 1533, 1477, 1331, 1300, 1219, 1180, 1038, 1013  $\text{cm}^{-1}$ .

$^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$ : 12.39 (1H, br s), 12.16 (1H, br s), 8.66 (1H, d,  $J=5.8\text{Hz}$ ), 7.86 (1H, d,  $J=1.5\text{Hz}$ ), 7.70 (1H, d,  $J=8.7\text{Hz}$ ), 7.63 (1H, d,  $J=2.5\text{Hz}$ ), 7.29-7.35 (2H, m), 4.09 (2H, s), 3.96 (3H, s).

20     **EXAMPLE 109**

- METHYL [6-CHLORO-2-(3,5-DIMETHYL PYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE**

- The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-chloro-2-(penylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and 2-bromoacetyl-3,5-dimethylpyridine hydrobromide\*.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 11.43 (1H, br s), 8.43 (1H, s), 7.60 (1H, d,  $J=8.7\text{Hz}$ ), 7.51 (1H, s), 7.45 (1H, d,  $J=1.8\text{Hz}$ ), 7.12 (1H, dd,  $J=1.8, 8.7\text{Hz}$ ), 4.22 (2H, s), 3.69 (3H, s), 2.62 (3H, s), 2.43 (3H, s).

\*2-Bromoacetyl-3,5-dimethylpyridine hydrobromide was prepared as follows;

- 30     2-Acetyl-3,5-dimethylpyridine:

The title compound was prepared from 3,5-dimethylpyridinecarbonitrile (K.Takahashi et al., *J. Heterocycl. Chem.*, 1978, 15, 893) according to the procedure for preparing 2-acetyl-4-chloropyridine described in Example 33.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.32 (1H, s), 7.37 (1H, s), 2.69 (3H, s), 2.56 (3H, s), 2.36 (3H, s).

5    2-Bromoacetyl-3,5-dimethylpyridine hydrobromide:

The title compound was prepared from 2-acetyl-3,5-dimethylpyridine according to the method of H. McKennis, Jr., L.B.Turnbull, E.R.Bowman, and E.Tamaki (in *J.Org.Chem.*, 1963, 23, 383-387).

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 8.43 (1H, s), 7.69 (1H, s), 5.00 (2H, s), 2.52 (3H, s), 2.39 (3H,

10    s).

**EXAMPLE 110**

**[6-CHLORO-2-(3,5-DIMETHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 58 from methyl [6-chloro-2-(3,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 109).

MS (EI) m/z: 342 (M<sup>+</sup>).

m.p.: 199-200 °C.

IR (KBr) ν: 3279, 1705, 1639, 1526, 1238, 1177, 827, 797 cm<sup>-1</sup>.

20    <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.12 (1H, br s), 11.72 (1H, br s), 8.38 (1H, s), 7.74 (1H, d, J=8.6Hz), 7.68 (1H, s), 7.52 (1H, d, J=2.0Hz), 7.10 (1H, dd, J=1.8, 8.6Hz), 3.72 (2H, s), 2.38 (3H, s), 2.33 (3H, s).

**EXAMPLE 111**

**METHYL [5-CHLORO-2-(4-ETHYL-3-FLUOROPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-chloro-2-(penylsulfonylamino)cinnamate (Example 36, step 3) and 2-bromoacetyl-4-ethyl-3-fluoropyridine\*.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 11.29 (1H, br s), 8.45 (1H, d, J=4.8Hz), 7.64 (1H, d, J=1.8Hz),

30    7.44 (1H, t, J=4.8Hz), 7.38 (1H, d, J=8.9Hz), 7.29 (1H, dd, J=2.0, 8.7Hz), 4.21 (2H, s), 3.72 (3H, s), 2.81 (2H, q, J=7.6Hz), 1.31 (3H, t, J=7.6Hz).

\*2-Bromoacetyl-4-ethyl-3-fluoropyridine was prepared as follows;

4-Ethyl-3-fluoropyridine-*N*-oxide:

To a mixture of 4-ethyl-3-fluoropyridine (R.P.Dikinson et al., *Bioorg. Med. Chem. Lett.*, 1996, 6, 2031, 28.51 g, 205.9 mmol) and 30% hydrogen peroxide (30 ml) in acetic acid (300 ml) was heated at reflux temperature for 3h. After cooling to room temperature, the resulting mixture was concentrated. The residue was diluted in dichloromethane (300 ml) and dried ( $\text{MgSO}_4$ ). Removal of solvent gave 32.30 g (100%) of the title compound as an oil.

10       $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ ) d: 8.43-8.46 (1H, m), 8.08 (1H, d,  $J=6.1\text{Hz}$ ), 7.38 (1H, dd,  $J=6.6$ , 9.7Hz), 2.61 (2H, q,  $J=7.6\text{Hz}$ ), 1.17 (3H, t,  $J=7.6\text{Hz}$ ).

4-Ethyl-3-fluoro-2-pyridinecarbonitrile:

The title compound was prepared from 4-ethyl-3-fluoropyridine-*N*-oxide according to the procedure for preparing 4-chloro-2-pyridinecarbonitrile described in Example 33.

15       $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ) d: 8.42 (1H, d,  $J=4.8\text{Hz}$ ), 7.43 (1H, t,  $J=5.1\text{Hz}$ ), 2.78 (2H, q,  $J=7.6\text{Hz}$ ), 1.30 (3H, t,  $J=7.6\text{Hz}$ ).

2-Acetyl-4-ethyl-3-fluoropyridine:

The title compound was prepared from 4-ethyl-3-fluoro-2-pyridinecarbonitrile according to the procedure for preparing 2-acetyl-4-chloropyridine described in Example 33.

20       $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ) d: 8.376 (1H, d,  $J=4.6\text{Hz}$ ), 7.36 (1H, t,  $J=4.8\text{Hz}$ ), 2.76 (2H, q,  $J=7.6\text{Hz}$ ), 2.71 (3H, s), 1.28 (3H, t,  $J=7.6\text{Hz}$ ).

2-Bromoacetyl-4-ethyl-3-fluoropyridine:

The title compound was prepared from 2-acetyl-4-ethyl-3-fluoropyridine according to the procedure for preparing 2-bromoacetyl-4-ethylpyridine described in Example 57.

25       $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ) d: 8.38 (1H, d,  $J=4.6\text{Hz}$ ), 7.43 (1H, d,  $J=4.6\text{Hz}$ ), 4.75 (2H, s), 2.78 (2H, q,  $J=7.6\text{Hz}$ ), 1.29 (3H, t,  $J=7.6\text{Hz}$ ).

**EXAMPLE 112**

30      [5-CHLORO-2-(4-ETHYL-3-FLUOROPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

A stirred solution of methyl [5-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 111, 391.2 mg, 1.044 mmol) in acetic acid (12 ml) and 2N aqueous HCl (4 ml) was heated at reflux temperature for 24h. After cooling to room temperature, the resulting mixture was concentrated. The residue was diluted in THF (100 ml), dried ( $\text{MgSO}_4$ ) and concentrated. The crude product was purified by recrystallization to afford 349.2 mg (93 %) of the title compound.  
5 MS (EI) m/z: 361 ( $\text{M}^+$ ).  
MS (EI) m/z: 361 ( $\text{M}^+$ ).

m.p.: 208 °C.

IR (KBr)  $\nu$ : 3217, 1720, 1632, 1516, 1429, 1234, 1180, 1057  $\text{cm}^{-1}$ .

10  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$ : 11.78 (1H, br s), 8.35 (1H, d,  $J=4.8\text{Hz}$ ), 7.73 (1H, d,  $J=2.0\text{Hz}$ ), 7.56 (1H, t,  $J=5.1\text{Hz}$ ), 7.39 (1H, d,  $J=8.9\text{Hz}$ ), 7.22 (1H, dd,  $J=2.0, 8.9\text{Hz}$ ), 3.65 (2H, s), 2.65 (2H, q,  $J=7.6\text{Hz}$ ), 1.14 (3H, t,  $J=7.6\text{Hz}$ ).

### EXAMPLE 113

15 METHYL [6-CHLORO-2-(4-ETHYL-3-FLUOROPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-chloro-2-(penylsulfonylamino)cinnamate (step i of Example 8, Method A).

20  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 11.23 (1H, br s), 8.46 (1H, d,  $J=4.8\text{Hz}$ ), 7.60 (1H, d,  $J=2.0\text{Hz}$ ), 7.42-7.46 (2H, m), 7.10-7.14 (1H, m), 4.23 (2H, s), 3.71 (3H, s), 2.81 (2H, q,  $J=7.6\text{Hz}$ ), 1.31 (3H, t,  $J=7.7\text{Hz}$ ).

### EXAMPLE 114

[6-CHLORO-2-(3-ETHOXY-4-ETHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

25 The title compound was prepared according to the procedure described in Example 58 from methyl [6-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 113).

m.p.: 165 °C.

IR (KBr)  $\nu$ : 3300, 2974, 1705, 1645, 1529, 1339, 1178  $\text{cm}^{-1}$ .

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.65 (1H, br s), 8.32 (1H, d, J=4.6Hz), 7.73 (1H, d, J=8.9Hz), 7.47-7.52 (2H, m), 7.10 (1H, dd, J=1.8, 8.6Hz), 3.89 (2H, q, J=6.9Hz), 3.70 (2H, s), 2.72 (2H, q, J=7.6Hz), 1.13-1.26 (6H, m).

**EXAMPLE 115**

- 5    **METHYL [6-CHLORO-2-(3-CHLORO-4-ETHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-chloro-2-(penylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and 2-bromoacetyl-3-chloro-4-ethylpyridine hydrobromide\*.

- 10    <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 10.05 (1H, br s), 8.47 (1H, d, J=4.9Hz), 7.53 (1H, d, J=8.7Hz), 7.32-7.34 (2H, m), 7.05 (1H, dd, J=1.8, 8.7Hz), 3.79 (2H, s), 3.61 (3H, s), 2.83 (2H, q, J=7.6Hz), 1.28 (3H, t, J=7.6Hz).

\*2-Bromoacetyl-3-chloro-4-ethylpyridine hydrobromide was prepared as follows:  
3-Chloro-4-ethylpyridine-*N*-oxide:

- 15    The title compound was prepared from 3-chloro-4-ethylpyridine (F.Marsais et al., *J.Organomet.Chem.*, 1981, 216, 139) according to the procedure for preparing 4-ethyl-3-fluoropyridine-*N*-oxide described in Example 111.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 8.46 (1H, d, J=1.8Hz), 8.16 (1H, d, J=6.6Hz), 7.40 (1H, dd, J=1.8, 6.6Hz), 2.67 (2H, q, J=7.6Hz), 1.14-1.19 (3H, m).

- 20    3-Chloro-4-ethyl-2-pyridinecarbonitrile:

The title compound was prepared from 3-chloro-4-ethylpyridine-*N*-oxide according to the procedure for preparing 4-chloro-2-pyridinecarbonitrile described in Example 33.

- <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.50 (1H, d, J=4.9Hz), 7.41 (1H, t, J=4.9Hz), 2.84 (2H, q, J=7.4Hz), 1.30 (3H, t, J=7.6Hz).

2-Acetyl-3-chloro-4-ethylpyridine:

The title compound was prepared from 3-chloro-4-ethyl-2-pyridinecarbonitrile according to the procedure for preparing 2-acetyl-4-chloropyridine described in Example 33.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.41 (1H, d, J=4.8Hz), 7.29 (1H, d, J=4.8Hz), 2.83 (2H, q, J=7.6Hz), 2.67 (3H, s), 1.27 (3H, t, J=7.6Hz).

**2-Bromoacetyl-3-chloro-4-ethylpyridine hydrobromide:**

The title compound was prepared from 2-acetyl-3-chloro-4-ethylpyridine  
5 according to the procedure for preparing 2-bromo-4-methylpyridine hydrobromide  
described in step 2 of Example 31.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 8.55 (1H, d, J=4.9Hz), 7.66 (1H, d, J=4.8Hz), 4.93 (2H, s),  
2.82 (2H, q, J=7.3Hz), 1.21 (3H, t, J=7.4Hz).

**EXAMPLE 116**

10 **[6-CHLORO-2-(3-CHLORO-4-ETHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in  
Example 58 from methyl [6-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-  
3-yl]acetate (Example 115).

15 m.p.: 158 °C.

IR (KBr) ν: 3335, 1730, 1630, 1529, 1325, 1200 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.83 (1H, br s), 8.54 (1H, d, J=4.8Hz), 7.75 (1H, d, J=8.7Hz),  
7.63 (1H, d, J=4.9Hz), 7.46 (1H, s), 7.12 (1H, dd, J=1.8, 8.7Hz), 3.57 (2H, s), 2.82 (2H,  
q, J=7.4Hz), 1.25 (3H, t, J=7.4Hz).

20 **EXAMPLE 117**

**METHYL [5-CHLORO-2-(3-CHLORO-4-ETHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in  
Example 57 from methyl *trans*-5-chloro-2-(penylsulfonylamino)cinnamate (Example  
25 36, step 3) and 2-bromoacetyl-3-chloro-4-ethylpyridine hydrobromide (Preparation 15  
described in Example 115).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.87 (1H, br s), 8.50 (1H, d, J=4.9Hz), 7.64 (1H, s), 7.29-7.40  
(3H, m), 3.86 (2H, s), 3.63 (3H, s), 2.88 (2H, q, J=7.6Hz), 1.32 (3H, t, J=7.6Hz).

**EXAMPLE 118**

30 **[5-CHLORO-2-(3-CHLORO-4-ETHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 58 from methyl [5-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 117).

m.p.: 220 °C.

5 IR (KBr) v: 3341, 1695, 1626, 1533, 1458, 1429, 1229 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.88 (1H, br s), 8.54 (1H, d, J=4.9Hz), 7.82 (1H, s), 7.63 (1H, d, J=4.9Hz), 7.46 (1H, d, J=8.9Hz), 7.34 (1H, dd, J=2.0, 8.9Hz), 3.60 (2H, s), 2.82 (2H, q, J=7.4Hz), 1.25 (3H, t, J=7.4Hz).

#### EXAMPLE 119

10 METHYL [5-CHLORO-2-(4,6-DIMETHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-chloro-2-(phenylsulfonylamino)cinnamate (Example 36, step 3) and 2-bromoacetyl-4,6-dimethylpyridine\*.

15 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.73 (1H, br s), 7.98 (1H, s), 7.67 (1H, br s), 7.42 (1H, d, J=8.9Hz), 7.30 (1H, dd, J=1.8 and 8.7Hz), 7.22 (1H, s), 4.27 (2H, s), 3.73 (3H, s), 2.70 (3H, s), 2.43 (3H, s).

\* 2-Bromoacetyl-3,4-dimethylpyridine was prepared from 2-acetyl-4,6-dimethylpyridine (Sundberg et al., *J. Am. Chem. Soc.*, 1969, 91, 658) according to the

20 procedure for preparing 2-bromoacetyl-4-ethylpyridine described in Example 57.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.72 (1H, s), 7.19 (1H, s), 5.13 (2H, s), 2.55 (3H, s), 2.38 (3H, s).

#### EXAMPLE 120

[5-CHLORO-2-(4,6-DIMETHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

25 The title compound was prepared according to the procedure described in Example 58 from methyl [5-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 119).

MS (EI) m/z: 342 (M<sup>+</sup>).

m.p.: 233-235 °C.

30 IR (KBr) v: 3288, 2919, 1742, 1630, 1599, 1529, 1333, 1232, 1180, 1067, 772 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.99 (1H, br s), 7.69 (1H, s), 7.57 (1H, s), 7.52 (1H, d,

J=8.9Hz), 7.28 (1H, s), 7.18 (1H, dd, J=2.1, 8.9Hz), 3.87 (2H, s), 2.49 (3H, s), 2.27 (3H, s).

**EXAMPLE 121**

**METHYL [6-CHLORO-2-(4,6-DIMETHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and 2-bromoacetyl-4,6-dimethylpyridine (Preparation is described in Example 119).

10  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 12.69 (1H, br s), 7.98 (1H, s), 7.62 (1H, d, J=8.7Hz), 7.50 (1H, d, J=0.7Hz), 7.22 (1H, s), 7.12 (1H, dd, J=1.6, 8.6Hz), 4.30 (2H, s), 3.72 (3H, s), 2.70 (3H, s), 2.43 (3H, s).

**EXAMPLE 122**

**[6-CHLORO-2-(4,6-DIMETHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 58 from methyl [6-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 121).

MS (EI) m/z: 342 ( $\text{M}^+$ ).

20 m.p.: 219-220 °C.

IR (KBr)  $\nu$ : 3300, 1701, 1639, 1603, 1535, 1225, 1180  $\text{cm}^{-1}$ .

$^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$ : 11.95 (1H, br s), 7.62 (1H, d, J=8.7Hz), 7.58 (1H, d, J=1.6Hz), 7.56 (1H, s), 7.27 (1H, s), 6.96 (1H, dd, J=2.0, 8.7Hz), 3.87 (2H, s), 2.49 (3H, s), 2.26 (3H, s).

25 **EXAMPLE 123**

**METHYL [5,6-DICHLORO-2-(4-METHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE**

**STEP 1. Methyl *trans*-4,5-dichloro-2-nitrocinnamate**

The title compound was prepared according to the procedure described in step 30 1 of Example 36 from 4,5-dichloro-2-nitrobenzaldehyde (J. Kenneth et al., *J. Med Chem.*, 1968, 11, 946).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.20 (1H, s), 8.04 (1H, d, J=15.8Hz), 7.72 (1H, s), 6.36 (1H, d, J=15.8Hz).

**STEP 2. Methyl *trans*-2-amino-4,5-dichlorocinnamate**

The title compound was prepared according to the procedure described in step 5 2 of Example 36 from methyl *trans*-4,5-dichloro-2-nitrocinnamate (step 1).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.65 (1H, d, J=15.8Hz), 7.42 (1H, s), 7.26 (1H, s), 6.81 (1H, s), 6.28 (1H, d, J=15.8Hz).

**STEP 3. Methyl *trans*-4,5-dichloro-2-(phenylsulfonylamino)cinnamate**

The title compound was prepared according to the procedure described in step 10 1 of Example 8 (Method A) from methyl *trans*-2-amino-4,5-dichlorocinnamate (step 2).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.80-7.70 (2H, m), 7.60-7.40 (6H, m), 7.02 (1H, br s), 6.13 (1H, d, J=16.1Hz), 3.79 (3H, s).

**STEP 4. Methyl [(5,6-dichloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate**

The title compound was prepared according to the procedure described in 15 Example 57 from methyl *trans*-4,5-dichloro-2-(phenylsulfonylamino)cinnamate (step 3) and 2-bromoacetyl-4-methylpyridine hydrobromide (Preparation is described in step 2 of Example 31).

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.45 (1H, br s), 8.69 (1H, d, J=5.1Hz), 8.14 (1H, s), 8.00-7.93 (2H, m), 7.59 (1H, d, J=4.3Hz), 4.16 (2H, s), 3.59 (3H, s), 3.32 (3H, s).

**EXAMPLE 124**

**[5,6-DICHLORO-2-(4-METHYL PYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

The titled compound was prepared according to the procedure described in Example 58 from methyl [5,6-dichloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 123).

m.p.: 220-224°C.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.41 (1H, s), 12.20 (1H, br s), 8.69 (1H, d, J=5.1Hz), 8.11 (1H, s), 7.96-7.58 (2H, m), 7.58 (1H, d, J=4.8Hz), 4.08 (2H, s), 2.47 (3H, s).

**EXAMPLE 125**

**METHYL [5-METHYL-2-(4-METHYL PYRIDINE-2-CARBONYL)-1H-INDOL-3-**

YL]ACETATESTEP 1. Methyl *trans*-2-amino-5-methylcinnamate

The title compound was prepared according to the procedure described in step 2 of Example 36 from methyl *trans*-5-methyl-2-nitrocinnamate (C.Venkatasubban, 5 J.Annamalai Univ., 1933, 2, 227).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.82 (1H, d, J=15.8Hz), 7.20-7.19 (1H, m), 7.01-6.98 (1H, m), 6.63 (1H, d, J=8.2Hz), 6.35 (1H, d, J=15.8Hz), 3.83 (2H, m), 3.80 (3H, s), 2.24 (3H, s)

STEP 2. Methyl *trans*-5-methyl-2-(phenylsulfonylamino)cinnamate

The title compound was prepared according to the procedure described in step 10 1 of Example 8 (Method A) from methyl *trans*-2-amino-5-methylcinnamate (step 1).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.70-7.67 (2H, m), 7.55-7.38 (4H, m), 7.26-7.14 (3H, m), 6.55 (1H, br s), 6.14 (1H, d, J=16.0Hz), 3.77 (3H, s), 2.33 (3H, s)

STEP 3. Methyl [5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate

The title compound was prepared according to the procedure described in 15 Example 57 from methyl *trans*-5-methyl-2-(phenylsulfonylamino)cinnamate (step 2) and 2-bromoacetyl-4-methylpyridine hydrobromide (Preparation is described in step 2 of Example 31).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.32 (1H, br s), 8.61 (1H, d, J=5.0Hz), 8.17 (1H, s), 7.46 (1H, s), 7.40 (1H, d, J=8.6Hz), 7.33-7.32 (1H, m), 7.22-7.19 (1H, m), 4.31 (2H, s), 3.72 (3H, s), 2.46 (6H, m)

EXAMPLE 126[5-METHYL-2-(4-METHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in 25 Example 58 from methyl [5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 125).

m.p.: 220-226 °C.

IR (KBr) v: 3736, 3649, 1697, 1533, 1508, 1398, 1194, 802 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.08 (1H, br s), 8.69 (1H, d, J=4.8Hz), 7.94 (1H, s), 7.56-30 7.49 (3H, m), 7.17 (1H, dd, J=8.4Hz), 4.05 (2H, s), 2.46 (3H, s), 2.40 (3H, s).

**EXAMPLE 127****METHYL [5-FLUORO-2-(4-METHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE****STEP 1. Methyl *trans*-5-fluoro-2-nitrocinnamate**

5 The title compound was prepared according to the procedure described in step 1 of Example 36 from 5-fluoro-2-nitrobenzaldehyde.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.17-8.10 (2H, m), 7.32-7.19 (2H, m), 6.36 (1H, d, J=15.8Hz), 3.84 (3H, s).

**STEP 2. Methyl *trans*-5-fluoro-2-aminocinnamate**

10 The title compound was prepared according to the procedure described in step 2 of Example 36 from methyl *trans*-5-fluoro-2-nitrocinnamate (step 1).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.77 (1H, dd, J=15.8, 1.5Hz), 7.10-7.06 (1H, m), 6.94-6.87 (1H, m), 6.68-6.63 (1H, m), 6.33 (1H, d, J=15.8Hz), 3.85 (2H, m), 3.81 (3H, s).

**STEP 3. Methyl *trans*-5-fluoro-2-(phenylsulfonylamino)cinnamate**

15 The title compound was prepared according to the procedure described in step 1 of Example 8 (Method A) from methyl *trans*-5-fluoro-2-aminocinnamate (step 2).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.68-7.65 (2H, m), 7.55-7.49 (2H, m), 7.44-7.33 (3H, m), 7.18-7.13 (1H, m), 7.10-7.04 (1H, m), 6.10 (1H, d, J=15.8Hz), 3.78 (3H, s).

**STEP 4. Methyl [5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate**

20 The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-fluoro-2-(phenylsulfonylamino)cinnamate (step 3).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.46 (1H, br s), 8.58-8.56 (1H, m), 8.12 (1H, s), 7.43-7.39 (1H, m), 7.33-7.26 (2H, m), 7.14-7.06 (1H, m), 4.26 (2H, s), 3.74 (3H, s), 2.45 (3H, s).

**EXAMPLE 128****[5-Fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid**

The title compound was prepared according to the procedure described in Example 58 from methyl [5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 127).

m.p.: 223 °C (decomposed).

30 IR (KBr) v: 1705, 1643, 1570, 1277, 1227, 1204, 1186 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.28 (1H, br s), 8.70 (1H, d, J=4.9Hz), 7.95 (1H, s), 7.71-7.66 (1H, m), 7.58-7.52 (2H, m), 7.25-7.17 (1H, m), 4.06 (2H, s), 2.47 (3H, s).

#### EXAMPLE 129

#### METHYL [5-METHOXY-2-(4-METHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-

##### YL]ACETATE

##### STEP 1. Methyl *trans*-5-methoxy-2-nitrocinnamate

The title compound was prepared according to the procedure described in step 1 of Example 36 from 5-methoxy-2-nitrobenzaldehyde.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.21 (1H, d, J=15.8Hz), 8.16-8.12 (1H, m), 7.00-6.96 (2H, m), 10 6.30 (1H, d, J=15.8Hz), 3.93 (3H, s), 3.83 (3H, s).

##### STEP 2. Methyl *trans*-5-methoxy-2-aminocinnamate

The title compound was prepared according to the procedure described in step 2 of Example 36 from methyl *trans*-5-methoxy-2-nitrocinnamate (step 1).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.83 (1H, d, J=15.8Hz), 6.92-6.91 (1H, m), 6.82 (1H, dd, J=8.7, 2.8Hz), 6.66 (1H, d, J=8.7Hz), 6.35 (1H, d, J=15.8Hz), 3.80 (3H, s), 3.76 (3H, s)

##### STEP 3. Methyl *trans*-5-methoxy-2-(phenylsulfonylamino)cinnamate

The title compound was prepared according to the procedure described in step 1 of Example 8 (Method A) from methyl *trans*-5-methoxy-2-aminocinnamate (step 2).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.67-7.64 (2H, m), 7.54-7.37 (4H, m), 7.24 (1H, d, J=8.7Hz), 20 6.95 (1H, d, J=2.8Hz), 6.89 (1H, dd, J=8.7, 2.8Hz), 6.82 (1H, br s), 6.10 (1H, d, J=15.8Hz), 3.81 (3H, s), 3.77 (3H, s).

##### STEP 4. Methyl [5-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-methoxy-2-(phenylsulfonylamino)cinnamate (step 3).

25 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.38 (1H, br s), 8.61 (1H, d, J=4.9Hz), 8.17 (1H, s), 7.40 (1H, d, J=8.7Hz), 7.34-7.32 (1H, m), 7.08-7.03 (2H, m), 4.31 (2H, s), 3.88 (3H, s), 3.73 (3H, s), 2.47 (3H, s).

#### EXAMPLE 130

#### [5-METHOXY-2-(4-METHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-

##### YL]ACETIC ACID

The titled compound was prepared according to the procedure described in Example 58 from methyl [5-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 129).

m.p.: 235 °C (decomposed).

5 IR (KBr)  $\nu$ : 1701, 1638, 1595, 1528, 1448, 1423, 1340, 1279, 1263, 1234, 1223, 1192, 1111  $\text{cm}^{-1}$ .

$^1\text{H-NMR}$  (DMSO-d<sub>6</sub>)  $\delta$ : 12.11 (1H, br s), 8.69 (1H, d, J=4.9Hz), 7.95 (1H, s), 7.58-7.55 (2H, m), 7.18 (1H, m), 7.02-6.98 (1H, m), 4.07 (2H, s), 3.79 (3H, s), 2.46 (3H, s).

#### EXAMPLE 131

10 METHYL [6-METHOXY-2-(4-METHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE

##### STEP 1. Methyl *trans*-(4-methoxy-2-nitro)cinnamate

A mixture of 4-bromo-3-nitroanisole (4.177 g, 18.0 mmol), methyl acrylate (3.24 ml, 36.0 ml), palladium(II) acetate (606.1 mg, 2.7 mmol), triphenylphosphine (1.416 g, 5.4 mmol), triethylamine (3.76 ml, 27.0 mmol) in DMF (45.0 ml) was stirred at 130 °C for 4h. After cooling to ambient temperature, the mixture was concentrated. To the residue was added water (30 ml), and then the mixture was extracted with ethyl acetate-toluene (3:1, 40 ml). The aqueous layer was further extracted with ethyl acetate (2 x 30 ml). The combined organic layers were dried ( $\text{MgSO}_4$ ) and concentrated to afford 6.42g (quant.) of the title compound as an brown oil.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.07-6.97 (4H, m), 6.31 (1H, d, 15.8Hz), 3.90 (3H, s), 3.82 (3H, s).

##### STEP 2. Methyl *trans*-2-amino-4-methoxycinnamate

The title compound was prepared according to the procedure described in step 2 of Example 36 from methyl *trans*-(4-methoxy-2-nitro)cinnamate (step 1).

25  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 7.80-6.21 (5H, m), 4.03 (2H, brs), 3.79 (6H, s).

##### STEP 3 . Methyl *trans*-4-methoxy-2-(*p*-toluenesulfonylamino)cinnamate

The title compound was prepared according to the procedure described in step 1 of Example 8 (Method A) from methy *trans*-4-methoxy-2-aminocinnamate (step 2).

30  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 7.62-6.73 (9H, m), 6.07 (1H, d, 15.8Hz), 3.80 (3H, s), 3.77 (3H, s), 2.37 (3H, s).

STEP 4. Methyl [6-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-methoxy-2-(*p*-toluenesulfonylamino)cinnamate (step 3) and 2-bromoacetyl-4-methylpyridine hydrobromide (Preparation is described in step 5 2 of Example 31).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.32 (1H, br s), 8.61 (1H, d, 4.94Hz), 8.19-7.55 (2H, m), 7.34-6.82 (3H, m), 4.31 (2H, s), 3.89 (3H, s), 3.72 (3H, s), 2.47 (3H, s).

**EXAMPLE 132****[6-METHOXY-2-(4-METHYL PYRIDINE-2-CARBONYL)-1H-INDOL-3-****YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl [6-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 131).

m.p.: 204 °C.

15 IR (KBr) v: 3198, 1709, 1630, 1593, 1531, 1460, 1423, 1334, 1275, 1213, 1161, 1136, 1039, 1001 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.11 (1H, br s), 8.68 (1H, d, 4.94Hz), 7.94 (1H, m), 7.62 (1H, d, 8.88Hz), 7.56-7.52 (1H, m), 7.14 (1H, d, 2.30Hz), 6.76 (1H, dd, 8.88Hz, 2.30Hz), 4.05 (2H, s), 3.82 (3H, s), 2.47 (3H, s).

**EXAMPLE 133****METHYL [5-ETHYL-2-(4-METHYL PYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE****STEP 1. Methyl *trans*-5-ethyl-2-aminocinnamate**

A mixture of 2-bromo-4-ethylaniline (1.0 g, 5.10 mmol), methyl acrylate (1.15 ml, 12.74 mmol), palladium(II) acetate (137 mg, 0.61 mmol), tri-*o*-tolylphosphine (7.5 mg, 2.45 mmol), and triethylamine (2.5 ml) in acetonitrile (10 ml) was heated at 110 °C. After stirring for 2 h, methyl acrylate (0.6 ml, 6.37 mmol), palladium(II) acetate (69 mg, 0.30 mmol), tri-*o*-tolylphosphine (372 mg, 1.22 mmol), triethylamine (1.3 ml) were added and the mixture was stirred at 110 °C for 7 h. The solvent was removed 30 and the residue was diluted with ethyl acetate (100 ml), washed with water (100 ml), dried (MgSO<sub>4</sub>) and concentrated. The residue was purified by flash column

chromatography eluting with ethyl acetate/hexane (1:5/1:4) to afford 793 mg (75.8 %) of the title compound as yellow solids.

5       $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 7.83 (1H, d,  $J=15.8\text{Hz}$ ), 7.21 (1H, m), 7.04-7.01 (1H, m), 6.64 (1H, d,  $J=8.2\text{Hz}$ ), 6.36 (1H, d,  $J=15.8\text{Hz}$ ), 3.87 (2H, m), 3.80 (3H, s), 2.51 (2H, q,  $J=7.6\text{Hz}$ ), 1.19 (3H, t,  $J=7.6\text{Hz}$ ).

**STEP 2. Methyl *trans*-5-ethyl-2-(phenylsulfonylamino)cinnamate**

The title compound was prepared according to the procedure described in step 1 of Example 8 (Method A) from methyl *trans*-5-ethyl-2-aminocinnamate (step 1).

10      $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 7.70-7.48 (4H, m), 7.42-7.36 (2H, m), 7.29-7.26 (2H, m), 7.20-7.17 (2H, m), 6.14 (1H, d,  $J=15.8\text{Hz}$ ), 3.76 (3H, s), 2.62 (2H, q,  $J=7.6\text{Hz}$ ), 1.21 (3H, t,  $J=7.6\text{Hz}$ ).

**STEP 3. Methyl [5-ethyl-2-(4-methylpyridine-2-carbonyl)-1*H*-indol-3-yl]acetate**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-ethyl-2-(phenylsulfonylamino)cinnamate (step 2).

15      $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 12.32 (1H, br s), 8.59-8.57 (1H, m), 8.14 (1H, m), 7.47-7.39 (2H, m), 7.30-7.21 (2H, m), 4.32 (2H, s), 3.73 (3H, s), 2.75 (2H, q,  $J=7.6\text{Hz}$ ), 2.43 (3H, s), 1.27 (3H, t,  $J=7.6\text{Hz}$ )

**EXAMPLE 134**

**[5-ETHYL-2-(4-METHYLPYRIDINE-2-CARBONYL)-1*H*-INDOL-3-YL]ACETIC**

20     **ACID**

The title compound was prepared according to the procedure described in Example 58 from methyl [5-ethyl-2-(4-methylpyridine-2-carbonyl)-1*H*-indol-3-yl]acetate (Example 133).

m.p.: 215 °C (decomposed).

25     IR (KBr)  $\nu$ : 1701, 1638, 1597, 1535, 1443, 1420, 1398, 1331, 1279, 1236, 1205  $\text{cm}^{-1}$ .

$^1\text{H-NMR}$  (DMSO)  $\delta$ : 12.09 (1H, br s), 8.69 (1H, d,  $J=4.9\text{Hz}$ ), 7.94 (1H, m), 7.58-7.51 (3H, m), 7.23-7.20 (1H, m), 4.06 (2H, s), 2.69 (2H, q,  $J=7.6\text{Hz}$ ), 2.46 (3H, s), 1.23 (3H, t,  $J=7.6\text{Hz}$ ).

**EXAMPLE 135**

30     **METHYL [5-ETHYL-2-(4-ETHYLPYRIDINE-2-CARBONYL)-1*H*-INDOL-3-**

YL]ACETATE)

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-ethyl-2-(phenylsulfonylamino)cinnamate (Example 133, step 2) and 2-bromoacetyl-4-ethylpyridine (Preparation is described in Example 57).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.35 (1H, br s), 8.63 (1H, d, J=5.1Hz), 8.20 (1H, m), 7.48 (1H, s), 7.42 (1H, d, J=8.6Hz), 7.34 (1H, dd, J=5.1, 1.8Hz), 7.26-7.22 (1H, m), 4.32 (2H, s), 3.73 (3H, s), 2.76 (4H, q, J=7.6Hz), 1.30 (6H, t, J=7.6Hz)

EXAMPLE 136

10 [5-ETHYL-2-(4-ETHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in Example 58 from methyl [5-ethyl-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 135).

15 m.p.: 206.2 °C.

IR (KBr) ν: 1703, 1636, 1595, 1533, 1431, 1333, 1283, 1236, 1188, 1117 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.09 (1H, br s), 8.73 (1H, d, J=4.9Hz), 7.97 (1H, s), 7.60-7.52 (3H, m), 7.22 (1H, d, J=8.6Hz), 4.06 (2H, s), 2.82-2.65 (4H, m), 1.28-1.21 (6H, m).

20 EXAMPLE 137

METHYL [6-ETHYL-2-(4-METHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE

STEP 1. Methyl *trans*-(4-acetyl-2-nitro)cinnamate

The title compound was prepared according to the procedure described in Example 131 from 4-bromo-3-nitroacetophenone and methyl acrylate .

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.58-8.10 (3H, m), 7.77-7.74 (1H, m), 6.48-6.42 (1H, m), 3.85 (3H, s), 2.68 (3H, s).

STEP 2. Methyl *trans*-4-(1-hydroxyethyl)-2-nitrocinnamate

To a solution of methyl *trans*-4-acetyl-2-nitrocinnamate (462.2 mg, 1.854 mmol) in methanol (55 ml) was added sodium borohydride (176.3 mg, 4.66 mmol) at room temperature. After stirring for 10 min, the mixture was concentrated. The

residue was diluted in dichloromethane (20 ml) and washed with brine (20 ml). The aqueous layer was extracted with dichloromethane (20 ml x 2). The combined organic layers were dried ( $\text{MgSO}_4$ ) and concentrated to afford 442 mg (quant.) of the title compound.

5      $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.12-6.33 (5H, m), 5.0 (1H, m), 3.83 (3H, s), 1.54 (3H, d, 9.56Hz).

STEP 3. Methyl *trans*-(4-ethyl-2-nitro)cinnamate

To a mixture of sodium iodide (1.668 g, 11.1 mmol) and acetonitrile (581  $\mu\text{l}$ , 11.1 mmol) was added chlorotrimethylsilane (1.41 ml, 11.1 mmol) at room temperature. After stirring for 10 min, a solution of methyl *trans*-4-(1-hydroxyethyl-2-nitro)cinnamate (563.6 mg, step 1) in hexane-toluene-acetonitrile (1:1:1, 6.0 ml) was added and the mixture was stirred for an additional 48h. The reaction mixture was diluted with toluene-ethyl acetate (2:3, 25 ml) and poured into water (25 ml). The organic layer was separated and washed with 5% aqueous sodium thiosulfate (30 ml), brine (30 ml) and dried ( $\text{MgSO}_4$ ). Removal of solvent gave 460 mg (quant.) of the title product as a brown oil.

15      $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.12-6.32 (5H, m), 3.83 (3H, s), 2.76 (2H, q, 7.59Hz), 1.29 (3H, t, 7.59Hz).

STEP 4. Methyl *trans*-2-amino-4-ethylcinnamate

The title compound was prepared according to the procedure described in step 20 2 of Example 36 from methyl *trans*-4-ethyl-2-nitrocinnamate (step 3).

15      $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 7.84-6.29 (5H, m), 3.80 (3H, s), 2.57 (2H, m), 1.21 (3H, t, 7.59Hz).

STEP 5. Methyl *trans*-4-ethyl-2-(*p*-toluenesulfonylamino)cinnamate

The title compound was prepared according to the procedure described in step 25 1 of Example 8 (Method A) from methyl *trans*-2-amino-4-ethylcinnamate (step 4).

15      $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 7.57 (2H, d, 8.40Hz), 7.46 (1H, d, 15.8Hz), 7.39-7.08 (5H, m), 6.43 (1H, s), 6.43 (1H, d, 15.8Hz), 3.78 (3H, s), 2.61 (2H, m), 2.37 (3H, s), 1.18 (3H, t, 7.75Hz).

STEP 6. Methyl [6-ethyl-2-(4-methylpridine-2-carbonyl)-1*H*-indol-3-

30     yl]acetate

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-ethyl-2-(*p*-toluenesulfonylamino)cinnamate (step 5) and 2-bromoacetyl-4-methylpyridine hydrobromide (Preparation is described in step 2 of Example 31).

- 5       $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 12.30 (1H, br s), 8.62 (1H, d, 4.94Hz), 8.18-7.32 (4H, m), 7.05-7.02 (2H, m), 4.33 (2H, s), 3.72 (3H, s), 2.79 (2H, q, 7.59Hz), 2.48 (3H, s), 1.31 (3H, t, 7.59Hz).

### EXAMPLE 138

- 10     [6-ETHYL-2-(4-METHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl [6-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 137).

m.p.: 204 -207 °C.

- 15     IR (KBr) v: 3240, 1709, 1636, 1593, 1531, 1394, 1204, 1144, 1001  $\text{cm}^{-1}$ .  
 $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 12.07 (1H, br s), 8.69 (1H, d, 4.94Hz), 7.93 (1H, m), 7.63 (1H, d, 8.40Hz), 7.55 (1H, m), 7.45 (1H, s), 7.00-6.96 (1H, m), 4.05 (2H, s), 2.73 (2H, q, 7.56Hz), 2.46 (3H, s), 1.24 (3H, t, 7.56Hz).

### EXAMPLE 139

- 20     METHYL [5-ISOPROPYL-2-(4-METHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE

#### STEP 1. Methyl *trans*-5-isopropyl-2-aminocinnamate

The title compound was prepared according to the procedure described in step 1 of Example 133 from 2-bromo-4-isopropylaniline.

- 25      $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 7.83 (1H, d, J=15.8Hz), 7.23 (1H, m), 7.08-7.05 (1H, m), 6.66 (1H, d, J=8.4Hz), 6.37 (1H, d, J=15.8Hz), 3.85 (2H, m), 3.81 (3H, s), 2.84-2.76 (1H, m), 1.21 (6H, m).

#### STEP 2. Methyl *trans*-5-isopropyl-2-(phenylsulfonylamino)cinnamate

- 30     The title compound was prepared according to the procedure described in step 1 of Example 8 (Method A) from methyl *trans*-5-isopropyl-2-aminocinnamate (step 1).

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 7.71-7.68 (2H, m), 7.58 (1H, d, J=15.8Hz), 7.51-7.20 (6H, m).

7.09 (1H, br.s), 6.16 (1H, d, J=15.8Hz), 4.11 (3H, s), 2.94-2.83 (1H, m), 1.24-1.21 (6H, m).

**STEP 3. Methyl [5-isopropyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate**

The title compound was prepared according to the procedure described in  
5 Example 57 from methyl *trans*-5-isopropyl-2-(phenylsulfonylamino)cinnamate (step 2).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.33 (1H, br s), 8.61 (1H, d, J=5.1Hz), 8.17-8.16 (1H, m), 7.50-7.42 (2H, m), 7.33-7.26 (2H, m), 4.32 (2H, s), 3.73 (3H, s), 3.08-2.97 (1H, m), 2.46 (3H, s), 1.33-1.30 (6H, m).

**EXAMPLE 140**

10 **[5-ISOPROPYL-2-(4-METHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 58 from methyl [5-isopropyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 139).

15 m.p.: 213 °C (decomposed).

IR (KBr) ν: 1717, 1641, 1597, 1537, 1327, 1273, 1196 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.10 (1H, br s), 8.70 (1H, d, J=4.9Hz), 7.95-7.94 (1H, m), 7.59-7.54 (2H, m), 7.27 (1H, dd, J=8.6, 1.7Hz), 4.07 (2H, s), 3.03 (1H, m), 2.46 (3H, s), 1.27-1.25 (6H, m).

20 **EXAMPLE 141**

**METHYL [2-(4-METHYLPYRIDINE-2-CARBONYL)-6-TRIFLUOROMETHYL-1H-INDOL-3-YL]ACETATE**

**STEP 1. Methyl *trans*-2-amino-4-(trifluoromethyl)cinnamate**

The title compound was prepared according to the procedure described in step  
25 1 of Example 133 from 2-bromo-5-(trifluoromethyl)aniline.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.79 (1H, d, J=15.8Hz), 7.46-7.43 (1H, m), 7.00-6.94 (2H, m), 6.41 (1H, d, J=15.8Hz), 4.18 (2H, m), 3.82 (3H, m).

**STEP 2. Methyl *trans*-2-phenylsulfonylamino-4-(trifluoromethyl)cinnamate**

The title compound was prepared according to the procedure described in step  
30 1 of Example 8 (Method A) from methyl *trans*-2-amino-4-(trifluoromethyl)cinnamate  
(step 1).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.77-7.68 (2H, m), 7.65-7.53 (4H, m), 7.47-7.41 (3H, m), 6.24 (1H, d, J=15.8Hz), 3.80 (3H, s).

STEP 3. Methyl [2-(4-methylpyridine-2-carbonyl)-6-trifluoromethyl-1H-indol-3-yl]acetate

5 The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-2-phenylsulfonylamino-4-(trifluoromethyl)cinnamate (step 2).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.74 (1H, br s), 8.58 (1H, d, J=4.9Hz), 8.12 (1H, s), 7.81-7.74 (2H, m), 7.35-7.32 (2H, m), 4.32 (2H, s), 3.75 (3H, s), 2.46 (3H, s).

10 **EXAMPLE 142**

[2-(4-METHYL PYRIDINE-2-CARBONYL)-6-TRIFLUOROMETHYL-1H-INDOL-3-YL]ACETIC ACID

15 The title compound was prepared according to the procedure described in Example 58 from methyl [2-(4-methylpyridine-2-carbonyl)-6-trifluoromethyl-1H-indol-3-yl]acetate (Example 141).

m.p.: 210-220 °C.

IR (KBr) ν: 1697, 1651, 1599, 1537, 1506, 1339, 1283, 1196, 1103, 1055 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO) δ: 12.62 (1H, br s), 8.71 (1H, d, J=4.9Hz), 8.10 (1H, s), 7.90-7.97 (2H, m), 7.61-7.59 (1H, m), 7.39-7.36 (1H, m), 4.14 (2H, s), 2.48 (3H, s).

20 **EXAMPLE 143**

METHYL [5-*tert*-BUTYL-2-(4-METHYL PYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE

STEP 1. Methyl *trans*-5-*tert*-butyl-2-aminocinnamate

The title compound was prepared according to the procedure described in step 25 1 of Example 133 from 2-bromo-4-*tert*-butylaniline.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.85 (1H, d, 15.8Hz), 7.38 (1H, d, 2.30Hz), 7.23 (1H, dd, 8.56Hz, 2.30Hz), 6.67 (1H, d, 8.56Hz), 6.37 (1H, d, 15.8Hz), 3.87 (2H, br s), 3.81 (3H, s), 1.28 (9H,s).

STEP 2 . Methyl *trans*-5-*tert*-butyl-2-(*p*-toluenesulfonylamino)cinnamate

30 The title compound was prepared according to the procedure described in step

1 of Example 8 (Method A) from methyl *trans*-5-*tert*-butyl-2-aminocinnamate and *p*-toluenesulfonyl chloride.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.60-7.20 (8H, m), 6.53 (1H, s), 6.17 (1H, d, 15.8Hz), 3.79 (3H, s), 2.46 (3H, s), 1.29 (s, 9H).

5 **STEP 3. Methyl [5-*tert*-butyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate**

The compound was prepared according to the procedure described in Example of 57 from methyl *trans*-5-*tert*-butyl-2-(*p*-toluenesulfonylamino)cinnamate (step 2) and 2-bromoacetyl-4-methylpyridine hydrobromide (Preparation is described in step 2 of Example 31).

10 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.33 (1H, br s), 8.63 (1H, d, 4.94Hz), 8.18 (1H, m), 7.62-7.32 (4H, m), 4.43 (2H, s), 3.74 (3H, s), 2.47 (3H, s), 1.40 (s, 9H).

**EXAMPLE 144**

**[5-*tert*-BUTYL-2-(4-METHYL PYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

15 The compound was prepared according to the procedure described in Example 9 (Method B) from methyl [5-*tert*-butyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 143).

m.p.: 191 °C.

IR (KBr) v: 2963, 1717, 1645, 1597, 1533, 1437, 1281, 1211, 1080, 1032, 1003 cm<sup>-1</sup>.

20 <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.10 (1H, br s), 7.70 (1H, d, 5.1Hz), 7.95-7.44 (6H, m), 4.09 (2H, s), 2.46 (3H, s), 1.35 (9H, s).

**EXAMPLE 145**

**METHYL [2-(4-METHYL PYRIDINE-2-CARBONYL)-5-TRIFLUOROMETHOXY-1H-INDOL-3-YL]ACETATE**

25 **STEP 1. Methyl *trans*-2-amino-5-(trifluoromethoxy)cinnamate**

The title compound was prepared according to the procedure described in step 1 of Example 133 from 2-bromo-4-(trifluoromethoxy)aniline.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.74 (1H, d, 15.8Hz), 7.23-7.02 (2H, m), 6.68 (1H, d, 8.72Hz), 6.36 (1H, d, 15.8Hz), 4.00 (2H, br s), 3.81 (3H, s).

30 **STEP 2 . Methyl *trans*-2-*p*-toluenesulfonylamino-5-(trifluoromethoxy)cinnamate**

The title compound was prepared according to the procedure described in step 1 of Example 8 (Method A) from methyl *trans*-2-amino-5-(trifluoromethoxy)cinnamate (step 1) and *p*-toluenesulfonyl chloride.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.59-7.19 (8H, m), 6.76 (1H, s), 6.15 (1H, d, 15.8Hz), 3.80 (3H, s), 2.39 (3H, s).

STEP 3. Methyl [2-(4-methylpyridine-2-carbonyl)-5-trifluoromethoxy-1H-indol-3-yl]acetate

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-2-*p*-toluenesulfonylamino-5-(trifluoromethoxy)cinnamate (step 2) and 2-bromoacetyl-4-methylpyridine hydrobromide (Preparation is described in step 2 of Example 31).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.7 (1H, br s), 8.64 (1H, d, 5.10Hz), 8.19 (1H, m), 7.55-7.23 (4H, m), 4.30 (2H, s), 3.74 (3H, s), 2.49 (3H, s).

**EXAMPLE 146**

15 [2-(4-METHYL-2-PYRIDINE-2-CARBONYL)-5-TRIFLUOROMETHOXY-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl [2-(4-methylpyridine-2-carbonyl)]-5-trifluoromethoxy-1H-indol-3-yl]acetate (Example 145).

20 m.p.: 235-238 °C.

IR (KBr) v: 3248, 1701, 1645, 1597, 1537, 1447, 1420, 1333, 1259, 1203, 1115, 1034, 1003 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.40 (1H, br s), 8.71 (1H, d, 4.94Hz), 7.97-7.96 (1H, m), 7.80-7.30 (4H, m), 4.09 (2H, s), 2.47 (3H, s).

25 **EXAMPLE 147**

METHYL [2-(4-ETHYL PYRIDINE-2-CARBONYL)-5-TRIFLUOROMETHOXY-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-2-*p*-toluenesulfonylamino-5-(trifluoromethoxy)cinnamate (step 2 of Example 145) and 2-bromoacetyl-4-ethylpyridine (Preparation is described in Example 57).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.66 (1H, d, 4.97Hz), 8.22 (1H, br s), 7.55-7.26 (4H, m), 4.30 (2H, s), 3.74 (3H, s), 2.79 (2H, q, 7.59Hz), 1.32 (3H, t, 7.59Hz).

#### EXAMPLE 148

##### [2-(4-ETHYLPYRIDINE-2-CARBONYL)-5-TRIFLUOROMETHOXY-1H-INDOL-3-

##### YL]ACETIC ACID

The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl [2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethoxy-1H-indol-3-yl]acetate (Example 147).

m.p.: 223 °C.

10 IR (KBr) v: 3271, 1697, 1645, 1597, 1539, 1423, 1400, 1337, 1258, 1198, 1117, 1028, 1003 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.41 (1H, br s), 8.74 (1H, d, 4.94Hz), 7.99 (1H, m), 7.80-7.75 (2H, m), 7.63-7.30 (2H, m), 4.10 (2H, s), 2.78 (2H, q, 7.59Hz), 1.26 (3H, t, 7.59Hz).

#### EXAMPLE 149

##### METHYL [6-METHYL-2-(4-METHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE

##### STEP 1. Methyl *trans*-2-amino-4-methylcinnamate

The title compound was prepared according to the procedure described in step 2 of Example 36 from methyl *trans*-4-methyl-2-nitrocinnamate.

20 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.81 (1H, d, J=15.8Hz), 7.30-7.26 (1H, m), 6.60-6.57 (1H, m), 6.52 (1H, m), 6.31 (1H, d, J=15.8Hz), 3.92 (2H, br s), 3.79 (3H, s), 2.26 (2H, s).

##### STEP 2. Methyl *trans*-4-methyl-2-(phenylsulfonylamino)cinnamate

The title compound was prepared according to the procedure described in step 1 of Example 8 (Method A) from methyl *trans*-2-amino-4-methylcinnamate (step 1).

25 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.72-7.68 (2H, m), 7.55-7.49 (1H, m), 7.44-7.34 (4H, m), 7.26-7.22 (1H, m), 7.07-7.04 (1H, m), 6.62 (1H, br s), 6.12 (1H, d, J=15.8Hz), 3.76 (3H, s), 2.34 (3H, s).

##### STEP 3. Methyl [6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate

The title compound was prepared according to the procedure described in 30 Example 57 from methyl *trans*-4-methyl-2-(phenylsulfonylamino)cinnamate (step 2).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.26 (1H, br s), 8.61 (1H, d, J=4.9Hz), 8.17 (1H, m), 7.58 (1H, d, J=8.4Hz), 7.34-7.29 (2H, m), 7.01-6.98 (1H, m), 4.32 (2H, s), 3.72 (3H, s), 2.49 (3H, s), 2.47 (3H, s).

**EXAMPLE 150**

- 5 [6-METHYL-2-(4-METHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in Example 58 from methyl [6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 149).

- 10 m.p.: 208 °C (decomposed).

IR (KBr) v: 1707, 1638, 1593, 1531, 1277, 1205, 1142 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.02 (1H, br s), 8.68 (1H, d, J=4.9Hz), 7.93 (1H, s), 7.61 (1H, d, J=8.2Hz), 7.56-7.54 (1H, m), 7.42 (1H, s), 6.96-6.93 (1H, m), 4.04 (2H, s), 2.46 (3H, s), 2.43 (3H, s).

- 15 **EXAMPLE 151**

METHYL [2-(4-METHYLPYRIDINE-2-CARBONYL)-5-TRIFLUOROMETHYL-1H-INDOL-3-YL]ACETATE

**STEP 1. Methyl trans-2-amino-5-(trifluoromethyl)cinnamate**

- The title compound was prepared according to the procedure described in step 20 1 of Example 133 from 2-bromo-4-(trifluoromethyl)aniline.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.77 (1H, d, J=15.8Hz), 7.61 (1H, s), 7.39 (1H, d, J=8.4Hz), 6.73 (1H, d, J=8.4Hz), 6.41 (1H, dd, J=15.8, 1.5Hz), 4.29 (2H, m), 3.82 (3H, m).

**STEP 2. Methyl trans-2-phenylsulfonylamino-5-(trifluoromethyl)cinnamate**

- The title compound was prepared according to the procedure described in step 25 1 of Example 8 (Method A) from methyl *trans*-2-amino-5-(trifluoromethyl)cinnamate (step 1).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.79-7.76 (2H, m), 7.66 (1H, m), 7.60-7.44 (6H, m), 7.06 (1H, br s), 6.26 (1H, d, J=15.8Hz), 3.81 (3H, s).

**STEP 3. Methyl [2-(4-methylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-**

- 30 **yl]acetate**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-2-phenylsulfonylamino-5-(trifluoromethyl)cinnamate (step 2).

- <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.70 (1H, br s), 8.62 (1H, d, J=4.9Hz), 8.17 (1H, s), 8.00 (1H, s),  
5 7.61-7.54 (2H, m), 7.38-7.36 (1H, m), 4.34 (2H, s), 3.75 (3H, s), 2.48 (3H, s).

**EXAMPLE 152**

**[2-(4-METHYL PYRIDINE-2-CARBONYL)-5-TRIFLUOROMETHYL-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in  
10 Example 58 from methyl [2-(4-methylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetate (Example 151).

m.p.: 218-225 °C.

IR (KBr) v: 1697, 1645, 1599, 1541, 1337, 1277, 1202, 1161, 1111, 1053 cm<sup>-1</sup>.

- <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.52 (1H, br s), 8.71 (1H, d, J=4.9Hz), 8.23 (1H, s), 7.97 (1H,  
15 m), 7.85 (1H, d, J=8.9Hz), 7.62-7.58 (2H, m), 4.16 (2H, s), 2.48 (3H, s).

**EXAMPLE 153**

**METHYL [2-(4-ETHYL PYRIDINE-2-CARBONYL)-5-TRIFLUOROMETHYL-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in  
20 Example 57 from methyl *trans*-2-phenylsulfonylamino-5-(trifluoromethyl)cinnamate (step 2 of Example 151) and 2-bromoacetyl-4-ethylpyridine (Preparation is described in Example 57).

- <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.65 (1H, br s), 8.64 (1H, d, J=5.1Hz), 8.21 (1H, m), 8.01 (1H,  
s), 7.61-7.52 (2H, m), 7.40-7.37 (1H, m), 4.34 (2H, s), 3.76 (3H, s), 2.78 (2H, q,  
25 J=7.6Hz), 1.31 (3H, t, J=7.6Hz).

**EXAMPLE 154**

**[2-(4-ETHYL PYRIDINE-2-CARBONYL)-5-TRIFLUOROMETHYL-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in  
30 Example 58 from methyl [2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetate (Example 153).

m.p.: 203.6 °C.

IR (KBr)  $\nu$ : 1703, 1647, 1599, 1537, 1340, 1202, 1105, 1051 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 12.52 (1H, br s), 8.74 (1H, d, J=5.1Hz), 8.24 (1H, s), 8.00-7.99 (1H, m), 7.86 (1H, d, J=8.7Hz), 7.64-7.58 (2H, m), 4.16 (2H, s), 2.79 (2H, q, J=7.6Hz), 1.26 (3H, t, J=7.6Hz).

#### EXAMPLE 155

##### METHYL (2-BENZOYL-1H-INDOL-3-YL)ACETATE

###### STEP 1. Methyl *trans*-2-(phenylsulfonylamino)cinnamate

The title compound was prepared according to the procedure described in step 10 of Example 8 (Method A) from methyl *trans*-2-aminocinnamate.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 7.71-7.67 (2H, m), 7.58 (1H, d, J=15.8Hz), 7.52-7.32 (6H, m), 7.28-7.22 (1H, m), 7.08 (1H, br s), 6.15 (1H, d, J=15.8Hz), 3.78 (3H, s).

###### STEP 2. Methyl (2-benzoyl-1H-indol-3-yl)acetate

The title compound was prepared according to the procedure described in 15 Example 57 from methyl *trans*-2-(phenylsulfonylamino)cinnamate (step 1).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 8.91 (1H, br s), 7.80-7.77 (2H, m), 7.67-7.58 (2H, m), 7.53-7.48 (2H, m), 7.43-7.34 (2H, m), 7.21-7.15 (1H, m), 3.86 (2H, s), 3.65 (3H, s).

#### EXAMPLE 156

##### (2-BENZOYL-1H-INDOL-3-YL)ACETIC ACID

20 The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl (2-benzoyl-1H-indol-3-yl)acetate (Example 155). m.p.: 194-196 °C.

IR (KBr)  $\nu$ : 1713, 1597, 1541, 1450, 1402, 1267, 1180, 729 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 11.62 (1H, br s), 7.77-7.74 (2H, m), 7.69-7.66 (2H, m), 7.60-7.55 (2H, m), 7.48-7.45 (1H, m), 7.34-7.28 (1H, m), 7.13-7.08 (1H, m), 3.80 (2H, s)

#### EXAMPLE 157

##### METHYL [2-(4-CHLOROBENZOYL)-6-METHYL-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in 30 Example 57 from methyl *trans*-4-methyl-2-(phenylsulfonylamino)cinnamate (step 2 of Example 149) and 4-chlorophenacyl bromide.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.84 (1H, br s), 7.74-7.71 (2H, m), 7.53-7.45 (3H, m), 7.14 (1H, m), 7.03-7.00 (1H, m), 3.81 (2H, s), 3.65 (3H, s), 2.46 (3H, s).

**EXAMPLE 158**

**[2-(4-CHLOROBENZOYL)-6-METHYL-1H-INDOL-3-YL]ACETIC ACID**

5 The title compound was prepared according to the procedure described in Example 58 from methyl [2-(4-chlorobenzoyl)-6-methyl-1H-indol-3-yl]acetate (Example 157).

m.p.: 193-195 °C.

IR (KBr) ν: 3302, 1697, 1587, 1335, 1263, 1090, 999, 770 cm<sup>-1</sup>.

10 <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.47 (1H, br s), 7.76-7.73 (2H, m), 7.65-7.61 (2H, m), 7.57 (1H, d, J=8.4Hz), 7.23 (1H, s), 6.96-6.93 (1H, m), 3.79 (2H, s), 2.42 (3H, s).

**EXAMPLE 159**

**[2-(4-CHLOROBENZOYL)-5-METHYL-1H-INDOL-3-YL]ACETIC ACID**

**STEP 1. 2-(4-Chlorobenzoyl)-5-methyl-1-(phenylsulfonyl)indole**

15 The title compound was prepared according to the procedure described in step 2 of Example 2 (Method B) from 5-methyl-1-(phenylsulfonyl)indole (E.Wenkert, P.Moeller, and S.Piettre, *J.Am.Chem.Soc.*, **1988**, 110, 7188-7194) and 4-chlorobenzoyl chloride.

20 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.02-7.96 (3H, m), 7.96-7.88 (2H, m), 7.57-7.43 (5H, m), 7.33-7.25 (2H, m), 6.88 (1H, s), 2.41 (3H, s).

**STEP 2. 2-(4-Chlorobenzoyl)-5-methylindole**

The title compound was prepared according to the procedure described in step 3 of Example 2 (Method B) from 2-(4-chlorobenzoyl)-5-methyl-1-(phenylsulfonyl)indole (step 1).

25 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.43 (1H, br s), 7.94-7.91 (2H, m), 7.51-7.47 (3H, m), 7.37 (1H, d, J=8.4Hz), 7.21 (1H, dd, J=8.4, 1.5Hz), 7.04-7.03 (1H, m), 2.44 (3H, s).

**STEP 3. Diethyl α-acetoxy-[2-(4-chlorobenzoyl)-5-methyl-1H-indol-3-yl]malonate**

The title compound was prepared according to the procedure described in step 4 of Example 2 (Method B) from 2-(4-chlorobenzoyl)-5-methylindole (step 3).

30 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.74 (1H, br s), 7.79 (2H, d, J=8.4Hz), 7.67 (1H, s), 7.42 (2H, d,

J=8.4Hz), 7.27-7.24 (1H, m), 7.14-7.11 (1H, m), 4.24-4.16 (4H, m), 2.45 (3H, s), 1.28-1.18 (6H, m).

**STEP 4. Diethyl [2-(4-chlorobenzoyl)-5-methyl-1H-indol-3-yl]malonate**

The title compound was prepared according to the procedure described in step 5 of Example 2 (Method B) from diethyl  $\alpha$ -acetoxy-[2-(4-chlorobenzoyl)-5-methyl-1H-indol-3-yl]malonate (step 3).

$^1$ H-NMR (CDCl<sub>3</sub>)  $\delta$ : 8.80 (1H, br s), 7.73 (2H, d, J=8.4Hz), 7.54 (1H, s), 7.47 (2H, d, J=8.4Hz), 7.21-7.18 (1H, m), 7.13-7.10 (1H, m), 4.25-4.13 (4H, m), 2.42 (3H, s), 1.28-1.21 (6H, m).

**10 STEP 5. [2-(4-Chlorobenzoyl)-5-methyl-1H-indol-3-yl]acetic acid**

The title compound was prepared according to the procedure described in step 6 of Example 2 (Method B) from diethyl [2-(4-chlorobenzoyl)-5-methyl-1H-indol-3-yl]malonate (step 4).

m.p.: 194-197 °C.

**15 IR (KBr) v:** 3308, 1695, 1609, 1529, 1402, 1263, 1223, 1088, 1015 cm<sup>-1</sup>.

$^1$ H-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 12.18 (1H, br s), 11.49 (1H, s), 7.77-7.73 (2H, m), 7.66-7.62 (2H, m), 7.45 (1H, s), 7.35 (1H, d, J=8.6Hz), 7.15 (1H, dd, J=8.6, 1.5Hz), 3.81 (2H, s), 2.39 (3H, s).

**EXAMPLE 160**

**20 METHYL [6-METHOXY-2-(4-CHLOROBENZOYL)-1H-INDOL-3-YL] ACETATE**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-methoxy-3-(*p*-toluenesulfonylamino)cinnamate (step 3 of Example 131) and 4-chlorophenacyl bromide.

$^1$ H-NMR (CDCl<sub>3</sub>)  $\delta$ : 8.89 (1H, br s), 7.74-7.43 (5H, m), 6.86-6.77 (m, 2H), 3.85 (3H, s), 3.79 (3H, s), 3.65 (3H, s).

**EXAMPLE 161**

**[6-METHOXY-2-(4-CHLOROBENZOYL)-1H-INDOL-3-YL] ACETIC ACID**

The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl [6-methoxy-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetate (Example 160).

m.p. : 193 °C.

IR(KBr) v: 3308, 1701, 1628, 1603, 1526, 1427, 1335, 1271, 1205, 1148, 1092, 1032, 999 cm<sup>-1</sup>.

- 5      <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.43 (1H, brs), 7.75-7.56 (5H, m), 6.87 (1H, d, 2.13Hz), 7.76 (1H, dd, 8.88Hz, 2.13Hz), 3.80 (3H, s), 3.79 (2H, s).

**EXAMPLE 162**

**[2-(4-CHLOROBENZOYL)-6-TRIFLUOROMETHYL-1H-INDOL-3-YL]ACETIC ACID**

**STEP 1. 1-Phenylsulfonyl-6-(trifluoromethyl)indole**

- 10      To a stirred mixture of 6-(trifluoromethyl)indole (500 mg, 2.70 mmol), 50 % aqueous sodium hydroxide (5 ml), water (7 ml), and tetrabutylammonium bromide (87 mg, 0.27 mmol) was added a solution of phenylsulfonyl chloride (379 μl, 2.97 mmol) in toluene (5 ml) at room temperature. After stirring for 1 h, the organic layer was separated. The aqueous layer was extracted with ethyl acetate (50 ml). The combined organic layers were washed with saturated sodium bicarbonate (30 ml), water (30 ml), brine (30 ml), dried (MgSO<sub>4</sub>), and concentrated to give 835 mg (95%) of the title compound.
- 15

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.29 (1H, s), 7.91-7.88 (2H, m), 7.71 (1H, d, J=3.6Hz), 7.64-7.54 (2H, m), 7.49-7.44 (3H, m), 6.72 (1H, d, J=3.6Hz).

- 20      **STEP 2. 2-(4-Chlorobenzoyl)-1-phenylsulfonyl-6-(trifluoromethyl)indole**

The title compound was prepared according to the procedure described in step 2 of Example 2 (Method B) from 1-phenylsulfonyl-6-(trifluoromethyl)indole (step 1).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.42 (1H, s), 8.05-8.01 (2H, m), 7.92-7.89 (2H, m), 7.71-7.47 (7H, m), 6.95 (1H, s).

- 25      **STEP 3. 2-(4-Chlorobenzoyl)-6-(trifluoromethyl)indole**

The title compound was prepared according to the procedure described in step 3 of Example 2 (Method B) from 2-(4-chlorobenzoyl)-1-phenylsulfonyl-6-(trifluoromethyl)indole (step 2).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.53 (1H, br s), 7.99-7.95 (2H, m), 7.85-7.79 (2H, m), 7.56-7.53

- 30 (2H, m), 7.42-7.39 (1H, m), 7.19-7.18 (1H, m).

STEP 4. Diethyl  $\alpha$ -acetoxy-[2-(4-chlorobenzoyl)-6-(trifluoromethyl)-1H-indol-3-yl]malonate

The title compound was prepared according to the procedure described in step 4 of Example 2 (Method B) from 2-(4-chlorobenzoyl)-6-(trifluoromethyl)indole (step 5 3).

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 9.27 (1H, br s), 8.00 (1H, d,  $J=8.7\text{Hz}$ ), 7.78 (2H, d,  $J=8.6\text{Hz}$ ), 7.68 (1H, s), 7.45-7.39 (3H, m), 4.24-4.12 (4H, m), 1.74 (3H, s), 1.21-1.14 (6H, m).

STEP 5. Diethyl [2-(4-chlorobenzoyl)-6-(trifluoromethyl)-1H-indol-3-yl]malonate

The title compound was prepared according to the procedure described in step 10 5 of Example 2 (Method B) from diethyl  $\alpha$ -acetoxy-[2-(4-chlorobenzoyl)-6-trifluoromethyl)-1H-indol-3-yl]malonate (step 4).

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 9.37 (1H, br s), 7.83 (1H, d,  $J=8.6\text{Hz}$ ), 7.77-7.73 (2H, m), 7.51-7.48 (3H, m), 7.33-7.30 (1H, m), 5.27 (1H, s), 4.25-4.06 (4H, m), 1.31-1.15 (6H, m)

STEP 6. [2-(4-Chlorobenzoyl)-5-methyl-1H-indol-3-yl]acetic acid

15 The title compound was prepared according to the procedure described in step 6 of Example 2 (Method B) from diethyl [2-(4-chlorobenzoyl)-6-(trifluoromethyl)-1H-indol-3-yl]malonate (step 5).

m.p.: 155-160 °C.

IR (KBr) v: 3379, 1705, 1611, 1589, 1516, 1337, 1229, 1119, 1092, 1055  $\text{cm}^{-1}$

20  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$ : 12.09 (1H, br s), 7.96-7.93 (1H, m), 7.82-7.78 (3H, m), 7.68-7.64 (2H, m), 7.41-7.37 (1H, m), 3.86 (2H, s).

EXAMPLE 163

METHYL [2-(4-CHLOROBENZOYL)-5-ETHYL-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in 25 Example 57 from methyl *trans*-5-ethyl-2-(phenylsulfonylamino)cinnamate (Example 133, step 2).

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.86 (1H, br s), 7.74-7.71 (2H, m), 7.48-7.41 (3H, m), 7.32-7.21 (2H, m), 3.85 (2H, s), 3.66 (3H, s), 2.75 (2H, q,  $J=7.6\text{Hz}$ ), 1.28 (3H, t,  $J=7.6\text{Hz}$ .)

EXAMPLE 164

30 [2-(4-CHLOROBENZOYL)-5-ETHYL-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in Example 58 from methyl [2-(4-chlorobenzoyl)-5-ethyl-1H-indol-3-yl]acetate (Example 163).

m.p.: 165-168 °C.

5 IR (KBr) : 3321, 1693, 1605, 1531, 1221, 1088, 1011 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.49 (1H, br s), 7.76-7.72 (2H, m), 7.65-7.61 (2H, m), 7.46 (1H, m), 7.36 (1H, d, J=8.6Hz), 7.18 (1H, dd, J=8.6, 1.5Hz), 3.81 (2H, s), 2.67 (2H, q, J=7.6Hz), 1.21 (3H, t, J=7.6Hz).

#### EXAMPLE 165

10 METHYL [2-(4-CHLOROBENZOYL)-5-METHOXY-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-methoxy-2-(phenylsulfonylamino)cinnamate (Example 129, step 3).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.81 (1H, br s), 7.75-7.72 (2H, m), 7.49-7.46 (2H, m), 7.29 (1H, d, J=8.9Hz), 7.04 (1H, dd, J=8.9, 2.5Hz), 6.98 (1H, d, J=2.5Hz), 3.86 (3H, s), 3.85 (2H, s), 3.67 (3H, s)

#### EXAMPLE 166

#### [2-(4-CHLOROBENZOYL)-5-METHOXY-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in Example 58 from methyl [2-(4-chlorobenzoyl)-5-methoxy-1H-indol-3-yl]acetate (Example 165).

m.p.: 200-204 °C.

IR (KBr) v: 3325, 1724, 1607, 1526, 1429, 1356, 1265, 1229, 1092, 1011 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.46 (1H, br s), 7.74 (2H, d, J=8.6Hz), 7.63 (2H, d, J=8.6Hz), 7.35 (1H, d, J=8.9Hz), 7.13 (1H, d, J=2.5Hz), 6.96 (1H, dd, J=8.9, 2.5Hz), 3.83 (2H, s), 3.77 (3H, s).

#### EXAMPLE 167

#### METHYL [2-(4-CHLOROBENZOYL)-5-ISOPROPYL-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-isopropyl-2-(phenylsulfonylamino)cinnamate (Example 139, step 2).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.87 (1H, br s), 7.74-7.70 (2H, m), 7.49-7.44 (3H, m), 7.33-7.25 (2H, m), 3.85 (2H, s), 3.66 (3H, s), 3.07-2.96 (1H, m), 1.32-1.29 (6H, m)

**EXAMPLE 168**

**[2-(4-CHLOROBENZOYL)-5-ISOPROPYL-1H-INDOL-3-YL]ACETIC ACID**

5 The title compound was prepared according to the procedure described in Example 58 from methyl [2-(4-chlorobenzoyl)-5-isopropyl-1H-indol-3-yl]acetate (Example 169).

m.p.: 197-200 °C.

IR (KBr) ν: 1697, 1609, 1533, 1429, 1348, 1265, 1090, 1011 cm<sup>-1</sup>.

10 <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.18 (1H, br s), 11.50 (1H, br s), 7.77-7.74 (2H, m), 7.65-7.62 (2H, m), 7.50 (1H, m), 7.40-7.37 (1H, m), 7.26-7.23 (1H, m), 3.83 (2H, s), 3.03-2.92 (1H, m), 1.26-1.24 (6H, m).

**EXAMPLE 169**

**METHYL [2-(4-CHLOROBENZOYL)-5-TRIFLUOROMETHYL-1H-INDOL-3-YL]ACETATE**

15 The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-2-phenylsulfonylamino-5-(trifluoromethyl)cinnamate (Example 151, step 2).

1 H-NMR (CDCl<sub>3</sub>) δ: 9.34 (1H, br s), 7.90 (1H, s), 7.77-7.70 (2H, m), 7.51-7.43 (2H, m), 7.33 (1H, d, J=8.7Hz), 3.85 (2H, s), 3.66 (3H, s)

**EXAMPLE 170**

**[2-(4-CHLOROBENZOYL)-5-TRIFLUOROMETHYL-1H-INDOL-3-YL]ACETIC ACID**

25 The title compound was prepared according to the procedure described in Example 58 from methyl [2-(4-chlorobenzoyl)-5-trifluoromethyl-1H-indol-3-yl]acetate (Example 169).

m.p.: 198-200 °C.

IR (KBr) ν: 3317, 1697, 1611, 1333, 1271, 1113, 1051, 1007 cm<sup>-1</sup>.

30 <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.08 (1H, br s), 8.18 (1H, s), 7.80-7.77 (2H, m), 7.68-7.57 (4H, m), 3.92 (2H, s).

**EXAMPLE 171****METHYL [2-(4-CHLOROBENZOYL)-5-TRIFLUOROMETHOXY-1H-INDOL-3-YL] ACETATE**

The title compound was prepared according to the procedure described in  
5 Example 57 from methyl *trans*-3-*p*-toluenesulfonylamino-5-(trifluoromethoxy)cinnamate (Example 145, step 2) and 4-chlorophenacyl bromide.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.93 (1H, br s), 7.76 (2H, d, 8.75Hz), 7.52-7.40 (5H, m), 3.82 (2H, s), 3.68 (3H, s).

**EXAMPLE 172****[2-(4-CHLOROBENZOYL)-5-TRIFLUOROMETHOXY-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl [2-(4-chlorobenzoyl)-5-trifluoromethoxy-1H-indol-3-yl]acetate (Example 171).

15 m.p.: 195 °C.  
IR (KBr) v: 3339, 1705, 1622, 1589, 1533, 1435, 1342, 1256, 1225, 1177, 1092, 1013 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.91 (1H, br s), 7.80-7.64 (5H, m), 7.55 (1H, d, 8.91Hz), 7.32-7.24 (m, 1H), 3.87 (2H, s).

**EXAMPLE 173****METHYL [6-CHLORO-2-(2-METHOXYBENZOYL)-1H-INDOL-3-YL]ACETATE**  
**STEP 1. Methyl 2-[6-chloro-2-(2-methoxybenzoyl)-1H-indol-3-yl]acetate**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans* 4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of  
25 Example 8, Method A) and 2-methoxyphenacyl bromide.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.02 (1H, br s), 7.60-7.46 (2H, m), 7.42-7.34 (2H, m), 7.15-6.99 (3H, m), 3.78 (3H, s), 3.66 (2H, s), 3.60 (3H, m).

**EXAMPLE 174****[6-CHLORO-2-(2-METHOXYBENZOYL)-1H-INDOL-3-YL]ACETIC ACID**

30 The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl [6-chloro-2-(2-methoxybenzoyl)-1H-indol-3-

yl]acetate (Example 172).

m.p.: 214-217 °C.

IR (KBr)  $\nu$ : 3398, 2939, 2642, 1711, 1680, 1624, 1537, 1461, 1315, 1230, 937 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 11.61 (1H, s), 7.67 (1H, d, J=8.7Hz), 7.60-7.51 (1H, m), 7.45 (1H, d, J=2.0Hz), 7.28 (1H, dd, J=7.4, 1.6Hz), 7.18 (1H, d, J=8.2Hz), 7.12-7.04 (2H, m), 3.70 (3H, s), 3.60 (2H, s).

#### **EXAMPLE 175**

##### **METHYL [6-CHLORO-2-(3-METHOXYBENZOYL)-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans* 4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and 3-methoxyphenacyl bromide.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 8.86 (1H, s), 7.57 (1H, d, J=8.7Hz), 7.46-7.26 (4H, m), 7.19-7.12 (2H, m), 3.86 (3H, s), 3.83 (2H, s), 3.67 (3H, s).

#### **EXAMPLE 176**

##### **[6-CHLORO-2-(3-METHOXYBENZOYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl [6-chloro-2-(3-methoxybenzoyl)-1H-indol-3-yl]acetate (Example 175).

m.p.: 227-231 °C.

IR (KBr)  $\nu$ : 3354, 2933, 2636, 1709, 1607, 1569, 1427, 1321, 1269, 1218, 1049 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 11.76 (1H, s), 7.72 (1H, d, J=8.6Hz), 7.54-7.45 (2H, m), 7.22 (3H, m), 7.16-7.10 (1H, m), 3.83 (3H, s), 3.79 (2H, s).

#### **EXAMPLE 177**

##### **METHYL [6-CHLORO-2-(3-BENZYLOXYBENZOYL)-1H-INDOL-3-**

##### **YL]ACETATE**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans* 4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and 3-benzyloxyphenacyl bromide (A.Hernandez et al., *J.Org.Chem.*, 1994, 59, 1058).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 8.79 (1H, s), 7.56 (1H, d, J=8.6Hz), 7.46-7.33 (9H, m), 7.26-7.19 (1H, m), 7.16 (1H, dd, J=8.6,1.8Hz), 5.12 (2H, s), 3.82 (2H, s), 3.64 (3H, s).

**EXAMPLE 178****[6-CHLORO-2-(3-BENZYLOXYBENZOYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl 2-[6-chloro-2-(3-benzyloxybenzoyl)-1H-indol-3-yl]acetate (Example 177).

m.p.: 174-177 °C.

IR (KBr) v: 3308, 3028, 2897, 1697, 1612, 1566, 1444, 1328, 1269, 1223, 732 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.76 (1H, s), 7.71 (1H, d, J=8.6Hz), 7.54-7.30 (10H, m), 7.13 (1H, dd, J=8.6,1.6Hz), 5.18 (2H, s), 3.78 (2H, s).

**EXAMPLE 179****METHYL [6-CHLORO-2-(3-HYDROXYBENZOYL)-1H-INDOL-3-YL]ACETATE**

A mixture of methyl [6-chloro-2-(3-benzyloxybenzoyl)-1H-indol-3-yl]acetate (Example 177, 0.37g, 0.85mmol) and 10% palladium-charcoal (80 mg) in ethyl acetate-methanol (5:1, 30 ml) was stirred under hydrogen atmosphere for 2.5 h. The mixture was filtered thorough a pad of Celite and the filtrate was concentrated. The solids were washed with dichloromethane (10 ml) to afford 70mg (24%) of the title compound as white solids.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 10.36 (1H, br s), 9.06 (1H, s), 7.55 (1H, d, J=8.7Hz), 7.50-7.46 (1H, m), 7.36-7.22 (3H, m), 7.15-7.05 (2H, m), 3.89 (2H, s), 3.65 (3H, s).

**EXAMPLE 180****[6-CHLORO-2-(3-HYDROXYBENZOYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl [6-chloro-2-(3-hydroxybenzoyl)-1H-indol-3-yl]acetate (Example 179).

m.p.: 213-215 °C.

IR (KBr) v: 3311, 3069, 1715, 1624, 1583, 1529, 1448, 1325, 1278, 1220, 761 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.71 (1H, s), 9.86 (1H, br s), 7.71 (1H, d, J=8.6Hz), 7.47 (1H, d, J=1.5Hz), 7.41-7.32 (1H, m), 7.20-7.02 (4H, m), 3.82 (2H, s).

**EXAMPLE 181**

**METHYL [6-CHLORO-2-(4-BENZYLOXYBENZOYL)-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans* 4-chloro-2-(phenylsulfonylamino)cinnamate (step i of Example 8, Method A) and 4-benzyloxyphenacyl bromide (A.Brossi et al., *J.Heterocycl.Chem.*, 1965, 2, 310).

- 5       $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.87 (1H, br s), 7.81 (2H, d,  $J=8.6\text{Hz}$ ), 7.55 (1H, d,  $J=8.7\text{Hz}$ ),  
7.48-7.32 (6H, m), 7.14 (1H, dd,  $J=8.7, 1.8\text{Hz}$ ), 7.06 (2H, d,  $J=8.6\text{Hz}$ ), 5.16 (2H, s),  
3.86 (2H, s), 3.65 (3H, s).

**EXAMPLE 182**

**[6-CHLORO-2-(4-BENZYLOXYBENZOYL)-1H-INDOL-3-YL]ACETIC ACID**

- 10     The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl 2-[6-chloro-2-(4-benzyloxybenzoyl)-1H-indol-3-yl]acetate (Example 181).

m.p.: 220-222 °C.

IR (KBr)  $\nu$ : 3331, 3013, 2914, 1717, 1699, 1599, 1564, 1508, 1253, 1167, 941  $\text{cm}^{-1}$ .

- 15      $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$ : 11.72 (1H, s), 7.76 (2H, d,  $J=8.9\text{Hz}$ ), 7.69 (1H, d,  $J=8.4\text{Hz}$ ),  
7.52-7.32 (6H, m), 7.17 (2H, d,  $J=8.9\text{Hz}$ ), 7.11 (1H, dd,  $J=8.4, 2.2\text{Hz}$ ), 5.23 (2H, s),  
3.81 (2H, s).

**EXAMPLE 183**

**METHYL [6-CHLORO-2-(4-HYDROXYBENZOYL)-1H-INDOL-3-YL]ACETATE**

- 20     The title compound was prepared according to the procedure described in Example 179 from methyl [6-chloro-2-(4-benzyloxybenzoyl)-1H-indol-3-yl]acetate (Example 181).

- 25      $^1\text{H-NMR}$  (acetone- $d_6$ )  $\delta$ : 10.82 (1H, br s), 9.21 (1H, br s), 7.75 (2H, d,  $J=8.7\text{Hz}$ ), 7.71  
(1H, d,  $J=8.7\text{Hz}$ ), 7.56 (1H, d,  $J=2.0\text{Hz}$ ), 7.13 (1H, dd,  $J=8.7, 2.0\text{Hz}$ ), 6.97 (2H, d,  
 $J=8.7\text{Hz}$ ), 3.95 (2H, s), 3.59 (3H, s).

**EXAMPLE 184**

**[6-CHLORO-2-(4-HYDROXYBENZOYL)-1H-INDOL-3-YL]ACETIC ACID**

- 30     The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl [6-chloro-2-(4-hydroxybenzoyl)-1H-indol-3-yl]acetate (Example 183).

m.p.: 231-234 °C.

IR (KBr)  $\nu$ : 3250, 3120, 2822, 1734, 1618, 1539, 1456, 1321, 1236, 1120, 1060  $\text{cm}^{-1}$ .

$^1\text{H-NMR}$  (DMSO-d<sub>6</sub>)  $\delta$ : 11.58 (1H, br s), 7.63-7.53 (3H, m), 7.35 (1H, d, J=1.9Hz), 7.00 (1H, dd, J=8.6,1.9Hz), 6.80 (2H, d, J=8.9Hz), 3.69 (2H, s).

5    **EXAMPLE 185**

METHYL [6-CHLORO-2-(4-ISOPROPOXYBENZOYL)-1H-INDOL-3-YL]ACETATE

To a stirred solution of methyl [6-chloro-2-(4-hydroxybenzoyl)-1H-indol-3-yl]acetate (Example 183, 0.15 g, 0.44 mmol) in DMF (5 ml) was added sodium hydride 10 (15 mg, 0.46 mmol) at room temperature under nitrogen atmosphere. After 5min., 2-iodopropane (78 mg) was added and the mixture was stirred for 7 h. The mixture was quenched with 2N aqueous HCl (20 ml), and extracted with ethyl acetate (50 ml). The extract was washed with water (30 ml) and brine (30 ml), dried ( $\text{MgSO}_4$ ), and concentrated. The residue was purified by flash column chromatography eluting with 15 ethyl acetate-hexane (1:2) to afford 72 mg (43%) of the title compound as white solids.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.81 (1H, br s), 7.80 (2H, d, J=8.9Hz), 7.56 (1H, d, J=8.7Hz), 7.41 (1H, d, J=1.8Hz), 7.15 (1H, dd, J=8.7,1.8Hz), 6.95 (2H, d, J=8.9Hz), 4.67 (1H, heptet, J=6.1Hz), 3.87 (2H, s), 3.67 (3H, s) 1.39 (6H, d, J=6.1Hz).

**EXAMPLE 186**

20    [6-CHLORO-2-(4-ISOPROPOXYBENZOYL)-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl [6-chloro-2-(4-isopropoxybenzoyl)-1H-indol-3-yl]acetate (Example 185).

m.p.: 216-218 °C.

25    IR (KBr)  $\nu$ : 3304, 2972, 2881, 1707, 1614, 1596, 1560, 1508, 1311, 1261, 1163  $\text{cm}^{-1}$ .

$^1\text{H-NMR}$  (DMSO-d<sub>6</sub>)  $\delta$ : 11.71 (1H, br s), 7.75 (2H, d, J=8.9Hz), 7.69 (1H, d, J=8.6Hz), 7.46 (1H, d, J=2.0Hz), 7.12 (1H, dd, J=8.6, 2.0Hz), 7.07 (2H, d, J=8.9Hz), 4.78 (1H, heptet, J=5.9Hz), 3.82 (2H, s) 1.32 (6H, d, J=5.9Hz).

**EXAMPLE 187**

30    METHYL [6-CHLORO-2-(4-PHENYLBENZOYL)-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in Example 57 from methyl *trans* 4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and 4-phenylphenacyl bromide.

5       $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.91 (1H, br s), 7.88 (2H, d,  $J=8.1\text{Hz}$ ), 7.73 (2H, d,  $J=8.1\text{Hz}$ ),  
7.68-7.38 (7H, m), 7.16 (1H, dd,  $J=8.1, 1.8\text{Hz}$ ), 3.89 (2H, s), 3.66 (3H, s).

**EXAMPLE 188**

**[6-CHLORO-2-(4-PHENYLBENZOYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl [6-chloro-2-(4-phenylbenzoyl)-1H-indol-3-yl]acetate (Example 187).

m.p.: 228-231 °C.

IR (KBr)  $\nu$ : 3317, 3030, 2868, 1707, 1620, 1600, 1527, 1431, 1323, 1256, 1194  $\text{cm}^{-1}$ .

10       $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$ : 11.81 (1H, s), 7.89 (2H, d,  $J=8.6\text{Hz}$ ), 7.87 (2H, d,  $J=8.6\text{Hz}$ ),  
7.82-7.72 (3H, m), 7.58-7.40 (4H, m), 7.14 (1H, dd,  $J=8.6, 1.8\text{Hz}$ ), 3.87 (2H, s).

15      **EXAMPLE 189**

**METHYL [6-CHLORO-2-(4-TRIFLUOROMETHOXYBENZOYL)-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans* 4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and 4-(trifluoromethoxy)phenacyl bromide\*.

10       $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.85 (1H, br s), 7.85 (2H, d,  $J=8.9\text{Hz}$ ), 7.57 (1H, d,  $J=8.6\text{Hz}$ ),  
7.40 (1H, d,  $J=1.8\text{Hz}$ ), 7.35 (2H, d,  $J=8.9\text{Hz}$ ), 7.16 (1H, dd,  $J=8.6, 1.8\text{Hz}$ ), 3.80 (2H, s),  
3.65 (3H, s).

\*4-(Trifluoromethoxy)phenacyl bromide was prepared as follows;

15      A mixture of 4-(trifluoromethoxy)acetophenone (0.52 g, 2.55 mmol) and tetrabutylammonium tribromide (1.35 , 2.80 mmol) in dichloromethane-methanol (1:1, 8 ml) was stirred for 18h and then concentrated. The residue was diluted with ethyl acetate (50 ml), washed with water ( 50 ml), brine (50 ml), and dried ( $\text{MgSO}_4$ ). Removal of solvent gave 0.36 g (50 %) of the title compound as a yellow oil.

20      tlc: Rf = 0.47 (hexane-ethyl acetate=10:1).

**EXAMPLE 190****[6-CHLORO-2-(4-TRIFLUOROMETHOXYBENZOYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in  
5 Example 9 (Method B) from methyl [6-chloro-2-(4-trifluoromethoxybenzoyl)1H-indol-3-yl]acetate (Example 189).

m.p.: 166-168 °C.

IR (KBr)  $\nu$ : 3315, 3219, 1719, 1699, 1616, 1527, 1508, 1254, 1221, 1167, 943 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 11.79 (1H, s), 7.88 (2H, d, J=8.6Hz), 7.75 (1H, d, J=8.9Hz),  
10 7.56 (2H, d, J=8.6Hz), 7.47 (1H, d, J=1.8Hz), 7.14 (1H, dd, J=8.9, 1.8Hz), 3.85 (2H, s).

**EXAMPLE 191****METHYL [5-CHLORO-2-(4-TRIFLUOROMETHOXYBENZOYL)-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in  
15 Example 8 (Method B) from methyl *trans* 5-chloro-2-(phenylsulfonylamino)cinnamate (Example 36, step 3) and 4-(trifluoromethoxy)phenacyl bromide (Preparation 18 described in Example 189).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 8.92 (1H, br s), 7.85 (2H, d, J=8.7Hz), 7.61 (1H, br s), 7.38-7.28  
(4H, m), 3.79 (2H, s), 3.67 (3H, s).

**EXAMPLE 192****[5-CHLORO-2-(4-TRIFLUOROMETHOXYBENZOYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in  
Example 9 (Method B) from methyl [5-chloro-2-(4-trifluoromethoxybenzoyl)-1H-  
25 indol-3-yl]acetate (Example 191).

m.p.: 186.7 °C.

IR (KBr)  $\nu$ : 3332, 3086, 2925, 1697, 1610, 1408, 1259, 1217, 1161, 1007, 941 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 11.85 (1H, br s), 7.89 (2H, d, J=8.7Hz), 7.81 (1H, d, J=2.1Hz),  
7.60-7.53 (2H, m), 7.48 (1H, d, J=8.7Hz), 7.32 (1H, dd, J=8.7, 2.1Hz), 3.86 (2H, s).

**EXAMPLE 193**

METHYL [5-CHLORO-2-(4-METHOXYBENZOYL)-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in Example 57 from methyl *trans* 5-chloro-2-(phenylsulfonylamino)cinnamate (Example 36, step 3) and 4-methoxyphenacyl bromide.

- 5   <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.86 (1H, s), 7.82 (2H, d, J=8.9Hz), 7.63-7.60 (1H, m), 7.37-7.26 (2H, m), 6.99 (2H, d, J=8.9Hz), 3.90 (3H, s), 3.84 (2H, s), 3.69 (3H, s).

**EXAMPLE 194**[5-CHLORO-2-(4-METHOXYBENZOYL)-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in  
10 Example 9 (Method B) from methyl [5-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetate (Example 193).

m.p.: 232-235 °C.

IR (KBr) ν: 3312, 2833, 2621, 1701, 1599, 1510, 1454, 1263, 1167, 1001, 777 cm<sup>-1</sup>.

- 15   <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.78 (1H, s), 7.78 (2H, d, J=8.9Hz), 7.75 (1H, d, J=2.0Hz),  
7.47 (1H, d, J=8.7Hz), 7.29 (1H, dd, J=8.7,2.0Hz), 7.11 (2H, d, J=8.9Hz), 3.88 (3H, s),  
3.82 (2H, s).

**EXAMPLE 195**METHYL [6-CHLORO-2-(4-NITROBENZOYL)-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in  
20 Example 57 from methyl *trans* 4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and 4-nitrophenacyl bromide.

15   <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.92 (1H, br s), 8.37 (2H, d, J=8.9Hz), 7.93 (2H, d, J=8.9Hz),  
7.57 (1H, d, J=8.7Hz), 7.40 (1H, d, J=1.8Hz), 7.18 (1H, dd, J=8.7,1.8Hz), 3.73 (2H, s),  
3.65 (3H, s).

**EXAMPLE 196**[6-CHLORO-2-(4-NITROBENZOYL)-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl [6-chloro-2-(4-nitrobenzoyl)-1H-indol-3-yl]acetate (Example 195).

- 30   m.p.: 218.9 °C (decomposed).

IR (KBr) v: 3365, 3101, 2846, 1718, 1699, 1647, 1537, 1348, 1255, 1227, 852 cm<sup>-1</sup>

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.84 (1H, s), 8.38 (2H, d, J=8.9Hz), 7.97 (2H, d, J=8.9Hz), 7.78 (1H, d, J=8.6Hz), 7.48 (1H, d, J=2.0Hz), 7.15 (1H, dd, J=8.6,2.0Hz), 3.83 (2H, s)

**EXAMPLE 197**

- 5 **METHYL [6-CHLORO-2-[(4-METHYLSULFONYL)BENZOYL]-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in Example 57 from 4-(methylsulfonyl)phenacyl bromide.

10 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.10 (1H, br s), 8.08 (2H, d, J=8.6Hz), 7.93 (2H, d, J=8.3Hz), 7.57 (1H, d, J=8.7Hz), 7.37 (1H, br), 7.20-7.10 m(1H, m), 3.78 (2H, s), 3.64 (3H, s), 3.12 (3H, s).

**EXAMPLE 198**

- [6-CHLORO-2-[(4-METHYLSULFONYL)BENZOYL]-1H-INDOL-3-YL]ACETIC ACID**

15 The title compound was prepared according to the procedure described in Example 9 (method B) from methyl [6-chloro-2-(4-methylsulfonyl)benzoyl-1H-indol-3-yl]acetate (Example 197).

m.p.: 241 °C (decomposed).

IR (KBr) v: 3330, 1713, 1614, 1524, 1230, 1150, 941, 781 cm<sup>-1</sup>.

20 <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.83 (1H, s), 8.12 (2H, d, J=8.3Hz), 7.96 (2H, d, J=8.3Hz), 7.78 (1H, d, J=8.7Hz), 7.48 (1H, d, J=1.8Hz), 7.15 (1H, dd, J=1.8, 8.7Hz), 3.85 (2H, s), 3.33 (3H, s).

**EXAMPLE 199**

- METHYL [6-CHLORO-2-[4-(METHYLSULFONYLAMINO)BENZOYL]-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in Example 8 (Method B) from methyl *trans*-4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and 4-(methylsulfonylamino)phenacyl bromide\*.

1 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.86 (1H, br s), 7.82 (2H, d, J=8.72Hz), 7.58 (1H, d, J=8.72Hz), 7.42- 7.15 (4H, m), 6.80 (1H, br s), 3.83 (2H, s), 3.67 (3H, s), 3.13 (3H, s).

\*4-(Methylsulfonylamino)phenacyl bromide was prepared from (4-

acetylphenyl)methanesulfonamide (R. Lis, et al., *J. Org. Chem.*, 1987, **52**, 4377) according to the procedure for preparing 4-(trifluoromethoxy)phenacyl bromide described in Example 189.

15       $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.01 (2H, d, 8.72Hz), 7.28 (2H, d, 8.72Hz), 4.40 (2H, s), 3.13 (2H,s)

**EXAMPLE 200**

**[6-CHLORO-2-[4-(METHYLSULFONYLAMINO)BENZOYL]-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in  
10      Example 9 (Method B) from methyl [6-chloro-2-[4-(methylsulfonylamino)benzoyl]-  
1H-indol-3-yl]acetate (Example 199).

m.p.: 207-210 °C.

IR (KBr) v: 3333, 3248, 1715, 1603, 1570, 1529, 1508, 1394, 1323, 1259, 1231, 1159,  
1061  $\text{cm}^{-1}$ .

15       $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$ : 11.6 (1H, br s), 7.76 (2H, d, J=8. 88Hz), 7.71 (1H, d,  
J=8.56Hz), 7.46 (1H, 1.65Hz), 7.12 (1H, dd, J=8.56Hz, 1.65Hz), 3.81 (2H, s), 3.13  
(3H, s).

**EXAMPLE 201**

**[6-CHLORO-2-(2-CHLOROBENZOYL)-1H-INDOL-3-YL]ACETIC ACID**

20      **STEP 1. 6-Chloro-2-(2-chlorobenzoyl)-1-(phenylsulfonyl)indole**

The title compound was prepared according to the procedure described in step  
2      2 of Example 1 (Method B) from 6-chloro-1-(phenylsulfonyl)indole (step 1 of  
Example 1, Method B) and 2-chlorobenzoyl chloride. The crude product was used for  
the next step without further purification.

25      tlc: Rf = 0.25 (hexane-ethyl acetate=4:1).

**STEP 2. 6-Chloro-2-(2-chlorobenzoyl)indole**

The title compound was prepared according to the procedure described in step  
3      3 of Example 1 (Method B) from 6-chloro-2-(2-chlorobenzoyl)-1-  
(phenylsulfonyl)indole (step 1). The crude product was used for the next step without  
30      further purification.

tlc: Rf = 0.37 (hexane-ethyl acetate=4:1)

STEP 3. Diethyl  $\alpha$ -acetoxy-2-[6-chloro-2-(2-chlorobenzoyl)-1H-indol-3-yl]malonate

The title compound was prepared according to the procedure described in step 4 of Example 1 (Method B) from 6-chloro-2-(2-chlorobenzoyl)indole (step 2).

- 1  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.61 (1H, br s), 7.79 (1H, d,  $J=8.88\text{Hz}$ ), 7.52-7.33 (5H, m), 7.15 (1H, dd,  $J=1.97\text{Hz}$ , 8.88Hz), 4.26 (4H, m), 2.02 (3H, s), 1.22 (6H, t,  $J=7.07\text{Hz}$ ).  
5

STEP 4. Diethyl [6-chloro-2-(2-chlorobenzoyl)-1H-indol-3-yl]malonate

The title compound was prepared according to the procedure described in step 5 of Example 1 (Method B) from diethyl  $\alpha$ -acetoxy-[6-chloro-2-(2-chlorobenzoyl)-1H-indol-3-yl]malonate (step 3).

- 10  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.95 (1H, br s), 7.75 (1H, d,  $J=8.88\text{Hz}$ ), 7.53-7.39 (5H, m), 4.83 (1H, s), 4.15 (4H, m), 1.20 (6H, t,  $J=7.26\text{Hz}$ ).

STEP 5. 2-[6-Chloro-2-(2-chlorobenzoyl)-1H-indol-3-yl]acetic acid

- The compound was prepared according to the procedure described in step 6 of Example 1 (Method B) from diethyl [6-chloro-2-(2-chlorobenzoyl)-1H-indol-3-yl]malonate (step 4).  
15

m.p.: 138-140 °C.

IR (KBr)  $\nu$ : 3315, 1713, 1632, 1564, 1526, 1435, 1325, 1254, 1215, 1151, 1061 cm<sup>-1</sup>.

$^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$ : 11.67 (1H, s), 7.61 (1H, d,  $J=8.72$ ), 7.51-7.34 (5H, m), 7.50 (1H, dd,  $J=1.97$ , 8.72Hz), 3.75 (2H, s).

20 **EXAMPLE 202**

[6-CHLORO-2-(2,4-DICHLOROBENZOYL)-1H-INDOL-3-YL]ACETIC ACIDSTEP 1. 6-Chloro-2-(2,4-dichlorobenzoyl)-1-(phenylsulfonyl)indole

- The title compound was prepared according to the procedure described in step 2 of Example 1 (Method B) from 6-chloro-1-(phenylsulfonyl)indole (step 1 of Example 1, Method B) and 2,4-dichlorobenzoyl chloride. The crude product was used for the next step without further purification.  
25

tlc:  $R_f = 0.34$  (hexane-ethyl acetate =4:1).

STEP 2. 6-Chloro-2-(2,4-dichlorobenzoyl)indole

- The title compound was prepared according to the procedure described in step 30 3 of Example 1 (Method B) from 6-chloro-2-(2,4-dichlorobenzoyl)-1-(phenylsulfonyl)indole (step 1). The crude product was used for the next step without

further purification.

tlc: R<sub>f</sub> = 0.45 (hexane-ethyl acetate =4:1)

**STEP 3. Diethyl α-acetoxy-[6-chloro-2-(2,4-dichlorobenzoyl)-1H-indol-3-yl]malonate**

The title compound was prepared according to the procedure described in step  
5 4 of Example 1 (Method B) from 6-chloro-2-(2,4-dichlorobenzoyl)indole (step 2).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.92 (1H, br s), 7.79-7.11(6H, m), 4.24 (4H, m), 2.02 (3H, s), 1.22 (6H, t, J=7.10Hz).

**STEP 4. Diethyl [6-chloro-2-(2,4-dichlorobenzoyl)-1H-indol-3-yl]malonate**

The title compound was prepared according to the procedure described in step  
10 5 of Example 1 from diethyl α-acetoxy-[6-chloro-2-(2,4-dichlorobenzoyl)-1H-indol-3-  
yl]malonate (step 3).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.92 (1H, br s), 7.75 (1H, d, J=8.92Hz), 7.55-7.36 (4H, m), 7.13 (1H, dd, 8.92Hz, 1.81Hz), 4.85 (1H, s), 4.17 (4H, m), 1.21 (6H, t, J=7.10Hz).

**STEP 5. [6-Chloro-2-(2,4-dichlorobenzoyl)-1H-indol-3-yl]acetic acid**

15 The title compound was prepared according to the procedure described in step  
6 of Example 1 (method B) from diethyl 2-[6-chloro-2-(2,4-dichlorobenzoyl)-1H-  
indol-3-yl]malonate (step 4).

m.p.: 190-192 °C.

IR (KBr) ν: 3304, 1709, 1630, 1589, 1526, 1427, 1321, 1231, 1150, 1061 cm<sup>-1</sup>.

20 <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.66 (1H, s), 7.72 (1H, d, J=2.00Hz), 7.64 (1H, d, 8.91Hz),  
7.51-7.33 (3H, m), 7.01 (1H, dd, J=2.00, 8.91Hz), 3.61 (2H, s).

**EXAMPLE 203**

**METHYL [6-CHLORO-2-(4-CHLORO-3-FLUOROBENZOYL)-1H-INDOL-3-  
YL]ACETATE**

25 The title compound was prepared according to the procedure described in  
Example 57 from methyl *trans*-4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of  
Example 8, Method A) and 4-chloro-3-fluorophenacyl bromide\* .

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.87 (1H, br s), 7.65-7.36 (4H, m), 7.17 (1H, dd, J=8.72Hz,  
1.81Hz), 3.80 (2H, s), 3.68 (3H, s).

30 4-chloro-3-fluorophenacyl bromide was prepared as follows;

4-Acetyl-1-chloro-2-fluorobenzene:

To a solution of 1-bromo-4-chloro-3-fluorobenzene (2.09g, 10mmol) in dry diethyl ether (12.0 ml) was added a solution of n-BuLi (1.55M in hexane, 6.77ml, 10.5mmol) at -78 °C under nitrogen atmosphere. The mixture was allowed to warm to -20 °C stirred for 45 min. A solution of *N,N*-dimethylacetamide (1.04 ml, 11.2 mmol) in diethyl ether (1.5 ml) was added and the mixture stirred for an additional 1h. The mixture was then allowed to warm to room temperature. After stirring for 3 h, the reaction mixture was poured into saturated aqueous ammonium chloride (20 ml) and extracted with diethyl ether (30 ml x 3). The combined organic layers were washed with 2N aqueous HCl (20 ml), saturated aqueous sodium bicarbonate (20 ml), brine (20 ml), and dried ( $\text{MgSO}_4$ ). Removal of solvent gave the title compound as a yellow oil (quant.).

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 7.75-7.09 (3H, m), 2.59 (3H,s).

**4-Chloro-3-fluorophenacyl bromide:**

The title compound was prepared from 4-acetyl-1-chloro-2-fluorobenzene according to the procedure for preparing 4-(trifluoromethoxy)phenacyl bromide described in Example 189.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 7.79-7.71 (2H, m), 7.58-7.52 (1H, m), 4.38 (2H,s).

**EXAMPLE 204**

**[6-CHLORO-2-(4-CHLORO-3-FLUOROBENZOYL)-1H-INDOL-3-YL]ACETIC ACID**

**20 ACID**

The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl [6-chloro-2-(4-methylsulfonylamino)phenacyl]-1H-indol-3-yl]acetate (Example 203).

m.p.: 179-182 °C.

25 MS (EI) m/z: 365 ( $\text{M}^+$ ).

$^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$ : 11.80 (1H, br s), 7.85-7.48 (5H, m), 7.14 (1H, dd,  $J=8.72\text{Hz}$ , 1.97Hz), 3.84 (2H, s).

**EXAMPLE 205**

**METHYL [6-CHLORO-2-(4-CYANOBENZOYL)-1H-INDOL-3-YL]ACETATE**

30 The title compound was prepared according to the procedure described in Example 8 (Method B) from methyl *trans*-4-chloro-2-(phenylsulfonylamino)cinnamate

(step 1 of Example 8, Method A) and 4-cyanophenacyl bromide.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.88 (1H, br s), 7.89-7.80 (4H, m), 7.58 (1H, d, J=8.75Hz), 7.41 (1H, d, 1.65Hz), 7.18 (1H, dd, 8.75Hz, 1.65Hz), 3.74 (2H, s), 3.36 (3H, s).

#### EXAMPLE 206

##### 5 METHYL [6-CHLORO-2-[4-(BROMO)BENZOYL]-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in Example 57 from methyl *trans* 4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and 4-bromophenacyl bromide.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.89 (1H, br s), 7.66 (4H, s), 7.55 (1H, d, J=8.6Hz), 7.36 (1H, d, J=1.6Hz), 7.15 (1H, dd, J=8.6,1.6Hz), 3.81 (2H, s), 3.66 (3H, s).

#### EXAMPLE 207

##### METHYL [6-CHLORO-2-[4-(2-THIENYL)BENZOYL]-1H-INDOL-3-YL]ACETATE

A mixture of methyl [6-chloro-2-(4-bromobenzoyl)-1H-indol-3-yl]acetate (Example 206, 0.40 g, 0.98 mmol), thiophene-2-boronic acid (0.14g, 1.08mmol), saturated aqueous sodium bicarbonate (4 ml), and dichlorobis(triphenylphosphine)palladium(II) (70 mg, 0.098 mmol) in DME (15 ml) was refluxed for 3h. The mixture was poured into water (30 ml), and extracted with ethyl acetate (50 ml x2). The combined extracts were washed with brine (50 ml), dried (MgSO<sub>4</sub>), and concentrated. The residue was purified by flash column chromatography eluting with ethyl acetate-hexane (1:6) to afford 0.33g (83 %) of the title compound as yellow solids.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.88 (1H, br s), 7.83 (2H, d, J=8.2Hz), 7.75 (2H, d, J=8.2Hz), 7.58 (1H, d, J=8.6Hz), 7.46 (1H, dd, J=3.6,1.2Hz), 7.42-7.38 (2H, m), 7.19-7.12 (2H, m), 3.87 (2H, s), 3.67 (3H, s).

#### EXAMPLE 208

##### [6-CHLORO-2-[4-(2-THIENYL)BENZOYL]-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl [6-chloro-2-[4-(2-thienyl)benzoyl]-1H-indol-3-yl]acetate (Example 207).

m.p.: 246-249 °C.

IR (KBr)  $\nu$ : 3319, 3068, 2628, 1705, 1610, 1593, 1427, 1323, 1257, 1186, 941 cm<sup>-1</sup>

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 11.79 (1H, s), 7.87 (2H, d, J=8.6Hz), 7.82 (2H, d, J=8.6Hz), 7.77-7.68 (3H, m), 7.48 (1H, d, J=1.5Hz), 7.26-7.20 (1H, m), 7.13 (1H, dd, J=8.6, 2.0Hz), 3.86 (2H, s).

5 **EXAMPLE 209**

**METHYL [6-CHLORO-2-[4-(2-FURYL)BENZOYL]-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in Example 207 from methyl [6-chloro-2-(4-bromobenzoyl)-1H-indol-3-yl]acetate (Example 206) and furan-2-boronic acid.

10 <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 8.90 (1H, br s), 7.83 (2H, d, J=8.7Hz), 7.80 (2H, d, J=8.7Hz), 7.60-7.54 (2H, m), 7.40 (1H, d, J=1.8Hz), 7.15 (1H, dd, J=8.6, 1.8Hz), 6.83 (1H, d, J=3.5Hz), 6.57-6.52 (1H, m), 3.86 (2H, s), 3.66 (3H, s).

**EXAMPLE 210**

**[6-CHLORO-2-[4-(2-FURYL)BENZOYL]-1H-INDOL-3-YL]ACETIC ACID**

15 The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl [6-chloro-2-[4-(2-furyl)benzoyl]-1H-indol-3-yl]acetate (Example 209).

m.p.: 230-232 °C.

IR (KBr)  $\nu$ : 3315, 2873, 2630, 1709, 1616, 1597, 1527, 1431, 1321, 1257, 1232 cm<sup>-1</sup>

20 <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 11.80 (1H, s), 7.93-7.79 (3H, m), 7.83 (2H, d, J=8.1Hz), 7.77 (1H, d, J=8.6Hz), 7.48 (1H, d, J=1.8Hz), 7.21 (1H, d, J=3.5Hz), 7.14 (1H, dd, J=8.6, 1.8Hz), 6.72-6.66 (1H, m), 3.84 (2H, s).

**EXAMPLE 211**

**METHYL [6-CHLORO-2-[4-(3-PYRIDYL)BENZOYL]-1H-INDOL-3-YL]ACETATE**

25 The title compound was prepared according to the procedure described in Example 207 from methyl [6-chloro-2-(4-bromobenzoyl)-1H-indol-3-yl]acetate (Example 206) and pyridine-3-boronic acid.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 8.95 (1H, br s), 8.90 (1H, d, J=2.5Hz), 8.69-8.65 (1H, m), 7.98-7.92 (1H, m), 7.92 (2H, d, J=8.6Hz), 7.73 (2H, d, J=8.6Hz), 7.59 (1H, d, J=8.7Hz), 7.48-7.40 (2H, m), 7.17 (1H, dd, J=8.7, 1.8Hz), 3.88 (2H, s), 3.67 (3H, s).

**EXAMPLE 212****[6-CHLORO-2-[4-(3-PYRIDYL)BENZOYL]-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl [6-chloro-2-[4-(3-pyridyl)benzoyl]-1H-indol-3-yl]acetate (Example 211).

m.p.: 194.8 °C.

IR (KBr)  $\nu$ : 3224, 2960, 1604, 1568, 1527, 1382, 1321, 1259, 1004, 920  $\text{cm}^{-1}$ .

$^1\text{H-NMR}$  ( $\text{CD}_3\text{OD}$ )  $\delta$ : 8.93-8.89 (1H, m), 8.57 (1H, dd,  $J=4.8, 1.5\text{Hz}$ ), 8.24-8.17 (1H, m), 7.98 (2H, d,  $J=8.6\text{Hz}$ ), 7.85 (2H, d,  $J=8.6\text{Hz}$ ), 7.68 (1H, d,  $J=8.6\text{Hz}$ ), 7.60-7.53 (1H, m), 7.46-7.42 (1H, m), 7.04 (1H, dd,  $J=8.6, 1.8\text{Hz}$ ), 3.67 (2H, s).

**EXAMPLE 213****METHYL [6-CHLORO-2-[4-(2-THIAZOLYL)BENZOYL]-1H-INDOL-3-YL]ACETATE**

To a stirred solution of thiazole (0.11 g, 1.23 mmol) in diethyl ether (4 ml) was added n-BuLi (1.55M in hexane, 0.79ml) at -78°C under nitrogen atmosphere. After stirring for 30 min., zinc chloride (1.0M in diethyl ether, 3.7 ml, 3.7 mmol) was added, and the mixture stirred at 0°C for 30 min. To the resulting mixture was added palladium catalyst prepared in THF (5 ml) by the treatment of a suspension of dichlorobis(triphenylphosphine)palladium(II) (0.22 g, 0.31mmol) with n-BuLi (1.55M in hexane, 0.39 ml). Methyl [6-chloro-2-(4-bromobenzoyl)-1H-indol-3-yl]acetate (Example 206, 0.25 g, 0.61 mmol) was added to the mixture. The reaction mixture was heated at reflux temperature for 4h., poured into water (50 ml), and extracted with ethyl acetate (50 ml). The combined extracts were washed with brine (50 ml), dried ( $\text{MgSO}_4$ ), and concentrated. This crude product was purified by flash column chromatography eluting with ethyl acetate-hexane (1:3) to afford 0.18g (72%) of the title compound as yellow solids.

$^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$ : 11.87 (1H, br s), 8.16 (2H, d,  $J=8.4\text{Hz}$ ), 8.04 (1H, d,  $J=3.1\text{Hz}$ ), 7.93 (1H, d,  $J=3.1\text{Hz}$ ), 7.86 (2H, d,  $J=8.4\text{Hz}$ ), 7.77 (1H, d,  $J=8.6\text{Hz}$ ), 7.49 (1H, d,  $J=1.6\text{Hz}$ ), 7.15 (1H, dd,  $J=8.6, 1.6\text{Hz}$ ), 3.97 (2H, s), 3.54 (3H, s).

**EXAMPLE 214****[6-CHLORO-2-[4-(2-THIAZOLYL)BENZOYL]-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl [6-chloro-2-[4-(2-thiazolyl)benzoyl]-1H-indol-3-yl]acetate (Example 213).

m.p.: 230-233 °C.

- 5 IR (KBr) v: 3331, 3126, 2546, 1693, 1635, 1535, 1350, 1313, 1213, 1150, 912 cm<sup>-1</sup>.  
<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.82 (1H, s), 8.15 (2H, d, J=8.6Hz), 8.04 (1H, d, J=3.3Hz), 7.93 (1H, d, J=3.3Hz), 7.88 (2H, d, J=8.6Hz), 7.75 (1H, d, J=8.7Hz), 7.49 (1H, d, J=2.0Hz), 7.14 (1H, dd, J=8.7,2.0Hz), 3.86 (2H, s).

#### EXAMPLE 215

10 **METHYL [6-CHLORO-2-(3-BROMOBENZOYL)-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans* 4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and 3-bromophenacyl bromide.

- 15 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.91 (1H, br s), 7.93-7.87 (1H, m), 7.77-7.67 (2H, m), 7.57 (1H, d, J=8.7Hz), 7.43-7.35 (2H, m), 7.19-7.13 (1H, m), 3.78 (2H, s), 3.69 (3H, s).

#### EXAMPLE 216

**METHYL [6-CHLORO-2-[3-(2-FURYL)BENZOYL]-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in Example 207 from methyl [6-chloro-2-(3-bromobenzoyl)-1H-indol-3-yl]acetate (Example 215) and furan-2-boronic acid.

- 17 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.93 (1H, br s), 8.05-8.01 (1H, m), 7.94-7.88 (1H, m), 7.68 (1H, m), 7.60-7.47 (3H, m), 7.45-7.41 (1H, m), 7.16 (1H, dd, J=8.6,1.6Hz), 6.74 (1H, d, J=3.3Hz), 6.52-6.47 (1H, m), 3.80 (2H, s), 3.57 (3H, s).

#### EXAMPLE 217

25 **[6-CHLORO-2-[3-(2-FURYL)BENZOYL]-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl [6-chloro-2-[3-(2-furyl)benzoyl]-1H-indol-3-yl]acetate (Example 216).

m.p.: 246-249 °C.

- 30 IR (KBr) v: 3310, 2984, 2632, 1695, 1624, 1568, 1327, 1227, 1062, 806, 739 cm<sup>-1</sup>.

- <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.81 (1H, s), 8.05-7.96 (2H, m), 7.82-7.77 (1H, m), 7.74 (1H,

d, J=8.7Hz), 7.68-7.61 (2H, m), 7.49 (1H, d, J=2.0Hz), 7.14 (1H, dd, J=8.7, 2.0Hz), 7.09 (1H, d, J=3.3Hz), 6.66-6.61 (1H, m), 3.83 (2H, s).

**EXAMPLE 218**

**METHYL *dl*-2-[6-CHLORO-2-(4-CHLOROBENZOYL)-1H-INDOL-3-YL]PROPIONATE**

**STEP 1. Methyl [1-*tert*-butoxycarbonyl-2-(4-chlorobenzoyl)-6-methyl-1H-indol-3-yl]acetate**

To a stirred suspension of methyl [2-(4-chlorobenzoyl)-6-methyl-1H-indol-3-yl]acetate (Example 8, Method B, 2.0 g, 5.5 mmol) in dichloromethane (20 ml) was added di-*tert*-butyl dicarbonate (2.4 g, 11mmol) and 4-dimethylaminopyridine (670 mg, 5.5 mmol) at room temperature. After stirring for 5 min, the mixture was poured into 10% citric acid (200 ml) and extracted with dichloromethane (200 ml). The extract was washed with water ( 200 ml), brine (200 ml), dried ( $\text{MgSO}_4$ ), and concentrated. The residue was purified by flash column chromatography eluting with ethyl acetate-hexane (1:4) to afford 2.3 g (90%) of the title compound as a yellow solids.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.26 (1H, d, J=2.2Hz), 7.74 (2H, d, J=8.6Hz), 7.53 (1H, d, J=8.6Hz), 7.44 (2H, d, J=8.6Hz), 7.32 (1H, dd, J=1.6, 8.4Hz), 3.72 (2H, s), 3.56 (3H, s), 1.30 (9H, s).

**STEP 2. Methyl [1-*tert*-butoxycarbonyl-2-(4-chlorobenzoyl)-6-methyl-1H-indol-3-yl]propionate**

To a stirred solution of methyl [1-*tert*-butoxycarbonyl-2-(4-chlorobenzoyl)-6-methyl-1H-indol-3-yl]acetate (step 1, 200 mg, 0.43 mmol) in THF (3 ml) was added a solution of lithium bis(trimethylsilyl)amide in THF (1 M, 0.5 ml) at -78 °C. After stirring for 0.5 h, iodomethane (0.14 ml, 2.2 mmol) was added at that temperature. The mixture was allowed to warm to -10 °C and stirred for an additional 0.5 h. The resulting mixture was poured into saturated aqueous ammonium chloride (50 ml) and extracted with diethyl ether (50 ml). The extract was washed with water (50 ml), brine (50 ml), dried ( $\text{MgSO}_4$ ) and concentrated. The residue was purified by TLC developing with ethyl acetate-hexane (1:4) to afford 146 mg (71 %) of the title compound as a colorless oil.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.28 (1H, d, J=1.9Hz), 7.75 (2H, d, J=8.4Hz), 7.59 (1H, d, J=8.4Hz), 7.44 (2H, d, J=8.6Hz), 7.28 (1H, dd, J=1.9, 8.4Hz), 3.86 (1H, q, J=7.3Hz), 3.54 (3H, s), 1.54 (3H, d, J=7.3Hz), 1.30 (9H, s).

STEP 3. Methyl *dl*-[2-(4-chlorobenzoyl)-6-methyl-1H-indol-3-yl]propionate

5       Methyl [1-*tert*-butoxycarbonyl-2-(4-chlorobenzoyl)-6-methyl-1H-indol-3-yl]propionate (step 2, 270 mg, 0.72 mmol) was dissolved in trifluoroacetic acid (5 ml). After siring for 10 min, the mixture was concentrated. To the residue was added saturated sodium bicarbonate (30 ml), and then the mixture was extracted with ethyl acetate (100 ml). The extract was washed with water (50 ml) brine (50 ml), dried 10 (MgSO<sub>4</sub>), and concentrated. The residue was purified by flash column chromatography eluting with ethyl acetate-hexane (1:3) to afford 210 mg (78%) of yellow solids.

15      <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.89 (1H, br), 7.78 (2H, d, J=8.7Hz), 7.67 (1H, d, J=8.7Hz), 7.50 (2H, d, J=8.6Hz), 7.40-7.37 (1H, m), 7.11 (1H, dd, J=1.8, 8.7Hz), 4.20 (1H, q, J=7.2Hz), 3.64 (3H, s), 1.54 (3H, d, J=7.2Hz).

EXAMPLE 219

*dl*-2-[2-(4-CHLOROBENZOYL)-6-CHLORO-1H-INDOL-3-YL]PROPIONIC ACID

The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl *dl*-[2-(4-chlorobenzoyl)-6-methyl-1H-indol-3-yl]propionate (Example 218).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.77 (1H, br s), 7.82 (2H, d, J=8.6Hz), 7.75 (1H, d, J=8.7Hz), 7.53 (2H, d, J=8.6Hz), 7.40 (1H, br), 7.13 (1H, dd, J=1.8, 8.7Hz), 4.20 (1H, q, J=7.2Hz), 1.61 (3H, d, J=7.2Hz).

EXAMPLE 220

25      METHYL [5-CHLORO-2-(ISOQUINOLINE-3-CARBONYL)-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-chloro-2-(phenylsulfonylamino)cinnamate (Example 36, step 3) and 3-bromoacetylisoquinoline hydrobromide\*.

30      <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.72 (1H, br s), 9.37 (1H, s), 8.80 (1H, s), 8.15-8.02 (2H, m), 7.87-7.76 (2H, m), 7.69 (1H, d, J=2.0Hz), 7.48 (1H, d, J=8.9Hz), 7.32 (1H, dd, J=2.0,

8.7Hz), 4.33 (2H, s), 3.76 (3H, s).

\* 3-Bromoacetylisoquinoline hydrobromide was prepared from 3-acetylisoquinoline (D. L. Klayman et al., *Arzneim. Forsch.*, 1986, 36, 10) according to the method of H.McKennis, Jr., L.B.Turnbull, E.R.Bowman, and E.Tamaki (in *J.Org.Chem.*, 1963, 28, 383-387).

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 9.49 (1H, s), 8.68 (1H, s), 8.34-8.26 (2H, m), 7.99-7.88 (2H, m), 5.14 (2H, s).

**EXAMPLE 221**

**[5-CHLORO-2-(ISOQUINOLINE-3-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

10 The title compound was prepared according to the procedure described in Example 58 from methyl [5-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetate (Example 219).

MS (EI) m/z: 364 (M<sup>+</sup>).

m.p.: 239-240 °C.

15 IR (KBr) ν: 3277, 1699, 1641, 1531, 1329, 1202, 1059, 961, 787 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.46 (1H, br s), 9.56 (1H, s), 8.69 (1H, s), 8.39-8.26 (2H, m), 7.99-7.90 (2H, m), 7.87 (1H, d, J=2.1Hz), 7.72 (1H, d, J=8.7Hz), 7.35 (1H, dd, J=2.1, 8.9Hz), 4.13 (2H, s)..

**EXAMPLE 222**

20 **METHYL [6-CHLORO-2-(ISOQUINOLINE-3-CARBONYL)-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and 3-bromoacetylisoquinoline (Preparation is described in Example 220).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.69 (1H, br s), 9.38 (1H, s), 8.81 (1H, s), 8.16-8.04 (2H, m), 7.88-7.77 (2H, m), 7.65 (1H, d, J=8.9Hz), 7.57 (1H, d, J=2.0Hz), 7.15 (1H, dd, J=2.0 and 8.7Hz), 4.36 (2H, s), 3.75 (3H, s).

**EXAMPLE 223**

30 **[6-CHLORO-2-(ISOQUINOLINE-3-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 58 from methyl [6-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetate (Example 222).

MS (EI) m/z: 364 ( $M^+$ ).

5 m.p.: 236-237 °C.

IR (KBr)  $\nu$ : 3229, 1709, 1641, 1618, 1531, 1198, 793  $\text{cm}^{-1}$ .

$^1\text{H-NMR}$  (DMSO-d<sub>6</sub>)  $\delta$ : 12.43 (1H, br s), 9.56 (1H, s), 8.70 (1H, s), 8.41-8.26 (2H, m), 7.99-7.87 (2H, m), 7.82 (1H, d, J=8.7Hz), 7.77 (1H, d, J=1.5Hz), 7.14 (1H, dd, J=2.0, 8.6Hz), 4.14 (2H, s).

10 **EXAMPLE 224**

**METHYL [5-CHLORO-2-(5-METHYLIPOXAZOLE-3-CARBONYL)-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-chloro-2-(phenylsulfonylamino)cinnamate (Example 15 36, step 3) and 3-bromoacetyl-5-methylisoxazole (M. D. Amici et al., *J. Org. Chem.* 1989, **54**, 2646).

$^1\text{H-NMR}$  (CDCl<sub>3</sub>)  $\delta$ : 10.75 (1H, br s), 7.68 (1H, br s), 7.42 (1H, d, J=8.2Hz), 7.33 (1H, dd, J=1.8, 9.1Hz), 6.60 (1H, s), 4.25 (2H, s), 3.74 (3H, s), 2.56 (3H, s).

**EXAMPLE 225**

**5-CHLORO-2-(5-METHYLIPOXAZOLE-3-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 58 from methyl [5-chloro-2-(5-methylisoxazole-3-carbonyl)-1H-indol-3-yl]acetate (Example 224).

25 MS (EI) m/z: 318 ( $M^+$ ).

m.p.: 253-255 °C.

IR (KBr)  $\nu$ : 3379, 1699, 1639, 1539, 1425, 1259, 1207, 1059, 804  $\text{cm}^{-1}$ .

$^1\text{H-NMR}$  (DMSO-d<sub>6</sub>)  $\delta$ : 11.76 (1H, br s), 7.81 (1H, d, J=2.0Hz), 7.59 (1H, d, J=8.9Hz), 7.29 (1H, dd, J=2.0, 8.7Hz), 6.67 (1H, s), 4.00 (2H, s), 2.49 (3H, s).

30 **EXAMPLE 226**

METHYL [6-CHLORO-2-(5-METHYLIPOXAZOLE-3-CARBONYL)-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of 5 Example 8, Method A) and 3-bromoacetyl-5-methylisoxazole (M. D. Amici et al., *J. Org. Chem.*, 1989, **54**, 2646).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 10.70 (1H, br s), 7.62 (1H, d, J=8.7Hz), 7.49 (1H, d, J=1.8Hz), 7.15 (1H, dd, J=1.8 and 8.7Hz), 6.60 (1H, br s), 4.27 (2H, s), 3.72 (3H, s), 2.56 (3H, s).

**EXAMPLE 227**

10 [6-CHLORO-2-(5-METHYLIPOXAZOLE-3-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in Example 58 from methyl [6-chloro-2-(5-methylisoxazole-3-carbonyl)-1H-indol-3-yl]acetate (Example 226).

15 MS (EI) m/z: 318 (M<sup>+</sup>).

m.p.: 227-229°C.

IR (KBr) v: 3331, 1713, 1645, 1543, 1404, 1259, 1202, 891, 804 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.70 (1H, br s), 7.74 (1H, d, J=8.7Hz), 7.62 (1H, d, J=1.3Hz), 7.07 (1H, dd, J=1.8, 8.6Hz), 6.67 (1H, br s), 4.01 (2H, s), 2.49 (3H, s).

20 **EXAMPLE 228**

METHYL [5-CHLORO-2-(4-METHYL-1,2,3-THIADIAZOLE-5-CARBONYL)-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-chloro-2-(phenylsulfonylamino)cinnamate (Example 25 36, step 3) and 5-bromoacetyl-4-methyl-1,2,3-thiadiazole hydrobromide\*.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.00 (1H, br s), 7.63 (1H, br s), 7.34 (1H, dd, J=1.8, 8.9Hz), 7.28 (1H, d, J=8.9Hz), 3.81 (2H, s), 3.66 (3H, s), 2.78 (3H, s).

\* 5-Bromoacetyl-4-methyl-1,2,3-thiadiazole hydrobromide was prepared as follows:

*N*-Methoxy-*N*-methyl-4-methyl-1,2,3-thiadiazole-5-carboxamide:

30 To a solution of 1,2,3-thiadiazole-5-carbonyl chloride (10.00 g, 61.5 mmol) and *N,O*-dimethylhydroxylamine hydrochloride (7.20 g, 73.8 mmol) in

dichloromethane (200 ml) was added triethylamine (20.6 ml, 147.6 mmol) at 0°C. After stirring for 2 h at room temperature, the mixture was diluted with dichloromethane (300 ml), washed with water (200 ml x 2) and dried ( $\text{MgSO}_4$ ). Removal of solvent gave 11.31 g (98%) of the title compound as brown crystals.

5      $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 3.75 (3H, s), 3.40 (3H, s), 3.01 (3H, s).

5-Acetyl-4-methyl-1,2,3-thiadiazole:

To a solution of *N*-methoxy-*N*-methyl-4-methyl-1,2,3-thiadiazole-5-carboxamide (11.31 g, 60.4 mmol) in THF (100 ml) was added 2M diethyl ether solution of methylmagnesium iodide (45.3 ml, 90.6 mmol) over 0.5 h at 0°C. The 10 mixture was allowed to warm to room temperature and stirred for 3 h.

The mixture was quenched with saturated aqueous ammonium chloride (100 ml) and then extracted with diethyl ether (200 ml x 2). The extracts were dried ( $\text{MgSO}_4$ ) and concentrated to give 7.49 g (87%) of the title compound as a pale brown oil.

15      $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 2.96 (3H, s), 2.67 (3H, s).

15     5-Bromoacetyl-4-methyl-1,2,3-thiadiazole:

To a solution of 5-acetyl-4-methyl-1,2,3-thiadiazole (1.00 g, 7.03 mmol) in chloroform (20 ml) was added dropwise a solution of bromine (1.24 g, 7.73 mmol) in chloroform (10 ml) over 0.5 h at room temperature. The mixture was heated at reflux temperature for 2 h. After cooling to room temperature, the mixture was made basic with saturated aqueous sodium bicarbonate and extracted with dichloromethane (100 ml x 2). The extracts were dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated to give 1.55 g (100%) of the title compound as a brown oil.

20      $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 4.28 (2H, s), 2.98 (3H, s).

**EXAMPLE 229**

25     [5-CHLORO-2-(4-METHYL-1,2,3-THIADIAZOLE-5-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

A mixture of methyl [5-chloro-2-(4-methyl-1,2,3-thiadiazole-5-carbonyl)-1H-indol-3-yl]acetate (Example 228, 190 mg, 0.54 mmol), 2N aqueous HCl (4 ml), and acetic acid (20 ml) was heated at reflux temperature for 2 h. After cooling to room 30 temperature, the mixture was concentrated. The crystalline residue was diluted with THF (100 ml) and dried ( $\text{MgSO}_4$ ) and concentrated. The residual solids were washed

with ethyl acetate gave 145 mg (79%) of the title compound as yellow solids.

MS (EI) m/z: 335 ( $M^+$ ).

m.p.: 229-230 °C.

IR (KBr)  $\nu$ : 3300, 1715, 1622, 1526, 1329, 1261, 1204, 1063, 1009, 822  $cm^{-1}$ .

5      $^1$ H-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 11.92 (1H, br s), 7.89 (1H, d, J=2.0Hz), 7.48 (1H, d, J=8.9Hz), 7.36 (1H, dd, J=2.0, 8.9Hz), 3.95 (2H, s), 2.63 (3H, s).

**EXAMPLE 230**

**METHYL [6-CHLORO-2-(4-METHYL-1,2,3-THIADIAZOLE-5-CARBONYL)-1H-INDOL-3-YL]ACETATE**

10       The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and 5-bromoacetyl-4-methyl-1,2,3-thiadiazole (Preparation is described in Example 228).

tlc: R<sub>f</sub>=0.56 (ethyl acetate/hexane=1:2)

15       **EXAMPLE 231**

**[6-CHLORO-2-(4-METHYL-1,2,3-THIADIAZOLE-5-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

20       The title compound was prepared according to the procedure described in Example 229 from methyl [6-chloro-2-(4-methyl-1,2,3-thiadiazole-5-carbonyl)-1H-indol-3-yl]acetate (Example 230).

MS (EI) m/z: 335 ( $M^+$ ).

m.p.: 215-216°C.

IR (KBr)  $\nu$ : 3300, 1709, 1645, 1531, 1327, 1211, 1065, 922, 789  $cm^{-1}$ .

25      $^1$ H-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 12.35 (1H, br s), 11.86 (1H, br s), 7.82 (1H, d, J=8.7Hz), 7.47 (1H, d, J=1.8Hz), 7.17 (1H, dd, J=1.8, 8.6Hz), 3.93 (2H, s), 2.63 (3H, s).

**EXAMPLE 232**

**METHYL [5-CHLORO-2-(5-METHYLTIAZOLE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE**

30       The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-chloro-2-(phenylsulfonylamino)cinnamate (Example 36, step 3) and 2-bromoacetyl-5-methylthiazole hydrobromide\*.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 11.74 (1H, br s), 7.76 (1H, d, J=1.1Hz), 7.67 (1H, d, J=1.8), 7.45 (1H, d, J=8.7Hz), 7.32 (1H, dd, J=2.0, 8.7Hz), 4.28 (2H, s), 3.73 (3H, s), 2.62 (3H, d, J=1.0Hz).

\* 2-Bromoacetyl-5-methylthiazole was prepared from 2-acetyl-5-methylthiazole 5 (Metzger et al., *Bull. Soc. Chim. Fr.*, 1953, 702) according to the method of H.McKennis, Jr., L.B.Turnbull, E.R.Bowman, and E.Tamaki (in *J.Org.Chem.*, 1963, 28, 383-387).

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 7.91 (1H, d, J=1.2Hz), 4.87 (2H, s), 2.58 (3H, d, J=0.8Hz).

#### EXAMPLE 233

10 [5-CHLORO-2-(5-METHYLTHIAZOLE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in Example 58 from methyl [5-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate (Example 232).

15 MS (EI) m/z: 334 (M<sup>+</sup>).

m.p.: 231-233°C.

IR (KBr) ν: 3348, 1699, 1630, 1541, 1404, 1333, 1271, 1057, 1003, 804 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.05 (1H, br s), 8.04 (1H, s), 7.88 (1H, br s), 7.77 (1H, d, J=8.7Hz), 7.35 (1H, br d, J=8.9Hz), 4.15 (2H, s), 2.63 (3H, s).

20 EXAMPLE 234

METHYL [6-CHLORO-2-(5-METHYLTHIAZOLE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and 2-bromoacetyl-5-methylthiazole (Preparation is described in Example 232).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 11.73 (1H, br s), 7.77 (1H, s), 7.62 (1H, d, J=8.2Hz), 7.51 (1H, br s), 7.14 (1H, br d, J=8.7Hz), 4.31 (2H, s), 3.72 (3H, s), 2.62 (3H, s).

#### EXAMPLE 235

30 [6-CHLORO-2-(5-METHYLTHIAZOLE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in Example 58 from methyl [6-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate (Example 234).

MS (EI) m/z: 334 ( $M^+$ ).

5 m.p.: 225-226°C.

IR (KBr)  $\nu$ : 3277, 1707, 1630, 1541, 1398, 1350, 1231, 1219, 1138, 878, 800  $cm^{-1}$ .

$^1$ H-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 12.25 (1H, br s), 11.99 (1H, br s), 8.04 (1H, s), 7.82 (1H, s), 7.81 (1H, d, J=9.0Hz), 7.13 (1H, br d, J=8.7Hz), 4.15 (2H, s), 2.63 (3H, s).

#### **EXAMPLE 236**

10 **[6-CHLORO-2-(2-THIENYL)CARBONYLINDOL-3-YL]ACETIC ACID**

##### **STEP 1. 6-Chloro-2-(2-thienylcarbonyl)-1-(phenylsulfonyl)indole**

The title compound was prepared according to the procedure described in step 2 of Example 2 (Method B) from 6-chloro-1-(phenylsulfonyl)indole (step 1 of Example 2, Method B) and 2-thienoyl chloride.

15  $^1$ H-NMR (CDCl<sub>3</sub>)  $\delta$ : 8.13-8.16 (3H, m), 7.77-7.80 (2H, m), 7.50-7.63 (4H, m), 7.29 (1H, dd, J=1.8, 8.4Hz), 7.19 (1H, t, J=5.4Hz), 7.03 (1H, s).

##### **STEP 2. 6-Chloro-2-(2-thienylcarbonyl)indole**

The title compound was prepared according to the procedure described in step 3 of Example 2 (Method B) from 6-chloro-2-(2-thienylcarbonyl)-1-(phenylsulfonyl)indole (step 1).

$^1$ H-NMR (CDCl<sub>3</sub>)  $\delta$ : 10.96 (1H, br s), 8.01 (1H, dd, J=1.2, 3.8Hz), 7.73 (1H, dd, J=1.2, 4.9Hz), 7.64 (1H, d, J=8.6Hz), 7.54-7.55 (1H, m), 7.35-7.37 (1H, m), 7.23 (1H, dd, J=3.8, 4.9Hz), 7.10 (1H, dd, J=1.8, 8.6Hz).

##### **STEP 3. Diethyl $\alpha$ -acetoxy-[6-chloro-2-(2-thienylcarbonyl)-1H-indol-3-yl]malonate**

25 The title compound was prepared according to the procedure described in step 4 of Example 2 (Method B) from 6-chloro-2-(2-thienylcarbonyl)indole (step 2).

$^1$ H-NMR (CDCl<sub>3</sub>)  $\delta$ : 8.93 (1H, br s), 7.82 (1H, d, J=8.9Hz), 7.76 (1H, d, J=4.9Hz), 7.55 (1H, d, J=3.8Hz), 7.39 (1H, d, J=1.8Hz), 7.11-7.18 (2H, m), 4.16-4.31 (4H, m), 1.87 (3H, s), 1.17-1.32 (6H, m).

30 **STEP 4. Diethyl [6-chloro-2-(2-thienylcarbonyl)-1H-indol-3-yl]malonate**

The title compound was prepared according to the procedure described in step 5 of Example 2 (Method B) from diethyl  $\alpha$ -acetoxyl[6-chloro-2-(2-thienylcarbonyl)-1H-indol-3-yl]malonate (step 3).

- 5       $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 9.27 (1H, br s), 7.71-7.75 (2H, m), 7.60-7.66 (1H, m), 7.05-7.17 (3H, m), 5.56 (1H, s), 4.07-4.26 (4H, m), 1.20-1.28 (6H, m).

STEP 5. [6-Chloro-2-(2-thienylcarbonyl)-1H-indol-3-yl]acetic acid

The title compound was prepared according to the procedure described in step 6 of Example 2 (Method B) from diethyl [6-chloro-2-(2-thienylcarbonyl)-1H-indol-3-yl]malonate (step 4).

- 10     MS (EI) m/z: 319 ( $\text{M}^+$ ).

m.p.: 177-178 °C.

IR (KBr)  $\nu$ : 3323, 1701, 1593, 1568, 1524, 1435, 1412, 1323, 1258, 1229, 920  $\text{cm}^{-1}$ .

- 15      $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$ : 12.25 (1H, br s), 11.85 (1H, br s), 8.13 (1H, d,  $J=4.9\text{Hz}$ ), 7.89 (1H, d,  $J=3.6\text{Hz}$ ), 7.74 (1H, d,  $J=8.7\text{Hz}$ ), 7.51 (1H, d,  $J=1.8\text{Hz}$ ), 7.34 (1H, t,  $J=4.8\text{Hz}$ ), 7.15 (1H, dd,  $J=1.8$ , 8.7Hz), 3.96 (2H, s).

EXAMPLE 237

METHYL [6-CHLORO-2-[3-(1-HYDROXY-1-METHYLETHYL)-2-FUROYL]-1H-INDOL-3-YL]ACETATE

The reaction was carried out according to the procedure described in Example

- 20     57 from methyl *trans*-4-chloro-2-(penylsulfonylamino)cinnamate (step 1 of Example 8 Method A) and 2-chloroacetyl-3-(1-hydroxy-1-methylethyl)furan\*.

15      $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 9.89 (1H, br s), 7.59 (1H, d,  $J=1.6\text{Hz}$ ), 7.53 (1H, d,  $J=8.7\text{Hz}$ ), 7.34 (1H, d,  $J=1.5\text{Hz}$ ), 7.08 (1H, dd,  $J=1.6$ , 8.7Hz), 6.57 (1H, d,  $J=1.8\text{Hz}$ ), 6.39 (1H, br s), 4.22 (2H, s), 3.73 (3H, s), 1.57 (6H, s).

- 25     \*2-Chloroacetyl-3-(1-hydroxy-1-methylethyl)furan was prepared as follows:  
To a solution of 2-(3-furyl)-2-propanol (T.M.Bargar et al., *J. Med. Chem.*, 1986, 29, 315., 2.0 g, 15.85 mmol) in THF (100 ml) was added a solution of n-butyllithium in hexane (1.55M, 30.7 ml, 47.55 mmol) at -78°C. After stirring for 1h, 2-chloro-N-methoxy-N-methylacetamide (6.54 g, 47.55 mmol) was added at 0°C. Saturated aqueous ammonium chloride (100 ml) was added to the mixture and the organic layer was separated. The organic layer was washed with water (100 ml x 2) and brine (50

ml) and dried ( $\text{MgSO}_4$ ). After removal of the solvent, the residue was purified by flash chromatography eluting with ethyl acetate/hexane (1:4) to afford 1.03 g (32%) of the title compound as an oil.

5      $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 7.52 (1H, d,  $J=1.8\text{Hz}$ ), 6.56 (1H, d,  $J=1.8\text{Hz}$ ), 5.51 (1H, s), 4.74 (2H, s), 1.56 (6H, s).

**EXAMPLE 238**

**[6-CHLORO-2-[3-(1-HYDROXY-1-METHYLETHYL)-2-FUROYL]-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in  
10 Example 58 from methyl [6-chloro-2-[3-(1-hydroxy-1-methylethyl)-2-furoyl]-1H-indol-3-yl]acetate (Example 237).

MS (EI) m/z: 361 ( $M^+$ ).

m.p.: 229-230°C.

IR(KBr)v: 3270, 2980, 1270, 1591, 1564, 1522, 1398, 1302, 1263, 1200, 785  $\text{cm}^{-1}$ .

15      $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$ : 11.78 (1H, br s), 7.97 (1H, d,  $J=1.6\text{Hz}$ ), 7.77 (1H, d,  $J=8.6\text{Hz}$ ), 7.56 (1H, d,  $J=1.5\text{Hz}$ ), 7.13 (1H, dd,  $J=1.8, 8.6\text{Hz}$ ), 6.87 (1H, d,  $J=1.6\text{Hz}$ ), 5.69 (1H, br s), 3.96 (2H, s), 1.53 (6H, s).

**EXAMPLE 239**

**METHYL [6-CHLORO-2-[3-METHOXYMETHYL-2-FUROYL]-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-chloro-2-(penylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and 2-chloroacetyl-3-(methoxymethyl)furan\*.

18      $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 9.81 (1H, br s), 7.60 (1H, d,  $J=1.6\text{Hz}$ ), 7.56 (1H, d,  $J=8.7\text{Hz}$ ), 7.40 (1H, d,  $J=1.5\text{Hz}$ ), 7.10 (1H, dd,  $J=1.8, 8.7\text{Hz}$ ), 6.79 (1H, d,  $J=1.6\text{Hz}$ ), 4.81 (2H, s), 4.26 (2H, s), 3.74 (3H, s), 3.48 (3H, s).

\*2-Chloroacetyl-3-(methoxymethyl)furan was prepared from 3-(methoxymethyl)furan (N.Greeves et al., *Synthesis*, 1993, 1109) according to the procedure for preparing 2-chloroacetyl-3-(1-hydroxy-1-methylethyl)furan described in Example 237.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.52 (1H, d, J=1.8Hz), 6.74 (1H, d, J=1.8Hz), 4.73 (2H, s), 4.62 (2H, s), 3.44 (3H, s).

#### EXAMPLE 240

##### [6-CHLORO-2-[3-METHOXYMETHYL-2-FUROYL]-1H-INDOL-3-YL]ACETIC ACID

###### 5    ACID

The title compound was prepared according to the procedure described in Example 58 from methyl [6-chloro-2-(3-methoxymethyl-2-furoyl)-1H-indol-3-yl]acetate (Example 239).

MS (EI) m/z: 347 (M<sup>+</sup>).

10    m.p.: 212-213°C.

IR (KBr) v: 3373, 3221, 1720, 1601, 1576, 1529, 1205, 1173, 1115, 1088 cm<sup>-1</sup>

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.72 (1H, br s), 8.04 (1H, d, J=1.6Hz), 7.76 (1H, d, J=8.7Hz), 7.59 (1H, d, J=1.5Hz), 7.12 (1H, dd, J=1.8, 8.7Hz), 6.86 (1H, d, J=1.6Hz), 4.70 (2H, s), 4.02 (2H, s), 3.36 (3H, s).

###### 15    EXAMPLE 241

##### [6-CHLORO-2-(1-METHYLMIDAZOLE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

###### STEP 1. Methyl [6-chloro-1-ethoxycarbonyl-2-(1-methylimidazole-2-carbonyl)indol-3-yl]acetate

20    The title compound was prepared according to the procedure described in step 2 of Example 31 from methyl *trans*-4-chloro-2-(ethoxycarbonylamino)cinnamate (Example 31, step 1) and 2-bromoacetyl-1-methylimidazole hydrobromide\*.

MS (EI) m/z: 405 (M<sup>+</sup>).

\*2-bromoacetyl-1-methylimidazole hydrobromide was prepared from 2-acetyl-1-methylimidazole according to the procedure for preparing 2-bromoacetyl-4-methylpyridine hydrobromide described in step 2 of Example 31.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 7.69 (1H, s), 7.27 (1H, s), 4.68 (2H, s); 3.81 (3H, s).

###### STEP 2. [6-chloro-1-ethoxycarbonyl-2-(1-methylimidazole-2-carbonyl)indol-3-yl]acetic acid

30    The title compound was prepared according to the procedure described in step 3 of Example 31 from methyl [6-chloro-1-ethoxycarbonyl-2-(1-methylimidazole-2-

carbonyl)indolin-3-yl]acetate (step 1).

m.p.: 235.5 °C.

IR (KBr)  $\nu$ : 3238, 1695, 1630, 1538, 1402, 1229, 1146  $\text{cm}^{-1}$ .

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 12.3 (1H, br s), 7.64 (1H, d,  $J=8.7\text{Hz}$ ), 7.50 (1H, d,  $J=1.8\text{Hz}$ ),

5 7.41 (1H, s), 7.16 (1H, s), 7.09 (1H, dd,  $J=1.8, 8.6\text{Hz}$ ), 4.25 (2H, s), 4.13 (3H, s).

#### EXAMPLE 242

##### METHYL [6-CHLORO-2-(1-METHYLMIDAZOLE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE

To a stirred solution of [6-chloro-2-(1-methylimidazole-2-carbonyl)indol-3-  
10 yl]acetic acid (Example 241, 65 mg, 0.21 mmol) in methanol (10 ml) was added (trimethylsilyl)diazomethane (1.0 M solution in hexanes, 1.05 ml, 2.1 mmol) at room temperature. After stirring for 19 h, the mixture was concentrated. The residue was purified by TLC developing with ethyl acetate-hexane (1:2) to afford 20 mg (23 %) of the title compound as yellow solids.

15  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 12.35 (1H, br s), 7.59 (1H, d,  $J=8.0\text{Hz}$ ), 7.49 (1H, d,  $J=1.5\text{Hz}$ ), 7.24 (1H, s), 7.11 (1H, dd,  $J=1.7, 8.1\text{Hz}$ ), 7.08 (1H, s), 4.30 (2H, s), 4.12 (3H, s), 3.71 (3H, s).

#### EXAMPLE 243

##### METHYL [5-CHLORO-2-(1-METHYLMIDAZOLE-2-CARBONYL)-1H-INDOL-3-

20 YL]ACETATE

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-chloro-2-(phenylsulfonylamino)cinnamate (Example 36, step 3) and 2-bromoacetyl-1-methylimidazole hydrobromide (Preparation is described in Example 241).

25  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$ : 12.28 (1H, br s), 7.85 (1H, s), 7.77 (1H, d,  $J=8.7\text{Hz}$ ), 7.66 (1H, s), 7.33-7.29 (2H, m), 4.21 (2H, s), 4.03 (3H, s), 3.60 (3H, s).

#### EXAMPLE 244

##### [5-CHLORO-2-(1-METHYLMIDAZOLE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

30 The title compound was prepared according to the procedure described in Example 58 from methyl [5-chloro-2-(1-methylimidazol-2-carbonyl)-1H-indol-3-

yl]acetate (Example 243).

m.p.: 230-233°C.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) d: 12.50 (1H, br s), 7.84 (1H, s), 7.76 (1H, d, J=13.2Hz), 7.66 (1H, s), 7.35-7.7.28 (2H, m), 4.15 (2H, s), 4.06 (3H, s).

5    **EXAMPLE 245**

**METHYL [5-CHLORO-2-(IMIDAZOLE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE**

**STEP 1. Methyl [5-chloro-2-[1-[2-(trimethylsilyl)ethoxymethyl]imidazole-2-carbonyl]-1H-indol-3-yl]acetate**

10       The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-chloro-2-(phenylsulfonylamino)cinnamate (Example 36, step 3) and 2-chloroacetyl-1-[2-(trimethylsilyl)ethoxymethyl]imidazole.\*

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) d: 12.38 (1H, br s), 7.66 (1H, s), 7.46-7.38 (2H, m), 7.34-7.29 (2H, m), 5.95 (2H, s), 4.29 (2H, s), 3.73 (3H, s), 3.66 (2H, t, J=8.0Hz), 0.98 (2H, t, J=8.0Hz),

15       0.03 (9H, s).

\*2-chloroacetyl-1-[2-(trimethylsilyl)ethoxymethyl]imidazole was prepared as follows.

To a stirred solution of 1-[2-(trimethylsilyl)ethoxymethyl]imidazole (Jeffrey P Whitten et al., *J. Org. Chem.*, **51**, 1891 (1986), 3.0 g, 15 mmol) in THF (30 ml) was added dropwise n-BuLi (1.55 M in n-hexane, 11.0 ml, 17 mmol) at -78 °C and the mixture was stirred for 1 h. To the resulting mixture was added 2-chloro-N-methoxy-N-methylacetamide (2.4 g, 17 mmol) at that temperature. The mixture was allowed to warm to 0°C and stirred at for an additional 2 h. The mixture was poured into water (50 ml) and extracted with ethyl acetate (80 ml), dried (MgSO<sub>4</sub>) and concentrated. The residual brown oil was purified by flash column chromatography eluting with ethyl acetate/hexane (1:4) to afford 1.2 g (32 %) of the title compound as a yellow oil.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) d: 7.39 (1H, s), 7.25 (1H, s), 5.81 (2H, s), 4.96 (2H, s), 3.60 (2H, t, J=8.2Hz), 0.95 (2H, t, J=8.2Hz), 0.02 (9H, s).

**STEP 2. Methyl [5-chloro-2-(imidazole-2-carbonyl)-1H-indol-3-yl]acetate**

To a solution of methyl [5-chloro-2-[1-[2-(trimethylsilyl)ethoxymethyl]imidazole-2-carbonyl]-1H-indol-3-yl]acetate (step 1, 300 mg, 0.67 mmol) in methanol (10 ml) was added 2N aqueous HCl (7 ml) and the

mixture was refluxed for 1.5 h. After cooling to room temperature, the mixture was concentrated. To the residue was added saturated aqueous sodium bicarbonate (10 ml) and then the mixture was concentrated. The residual yellow solids were dissolved in THF (100 ml) and dried ( $\text{MgSO}_4$ ). Removal of solvent afforded 220 mg  
5 (100%) of the title compound as yellow solids.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 12.16 (1H, br s), 10.80 (1H, br s), 7.68 (1H, s), 7.50-7.28 (5H, m),  
4.29 (2H, s), 3.70 (3H, s).

#### EXAMPLE 246

##### [5-CHLORO-2-(IMIDAZOLE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

10 The title compound was prepared according to the procedure described in Example 58 from methyl [5-chloro-2-(imidazole-2-carbonyl)-1H-indol-3-yl]acetate (Example 245).

m.p.: 253-254 °C.

15  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$ : 12.28 (1H, br s), 7.84 (1H, d,  $J=2.0\text{Hz}$ ), 7.80 (1H, d,  $J=9.1\text{Hz}$ ),  
7.32 (1H, dd,  $J=2.0, 9.1\text{Hz}$ ), 4.17 (2H, s).

#### EXAMPLE 247

##### METHYL [6-CHLORO-2-(IMIDAZOLE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE

20 STEP 1. Methyl [6-chloro-2-[1-[2-(trimethylsilyl)ethoxymethyl]imidazole-2-carbonyl]-1H-indol-3-yl]acetate

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-chloro-2-(phenylsulfonylamino)cinnamate (Step 1 of Example 8, Method A) and 2-chloroacetyl-1-[2-(trimethylsilyl)ethoxymethyl]imidazole (Preparation is described in step 1 of Example 245).

25  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 12.34, (1H, br s), 7.61 (1H, d,  $J=8.6\text{Hz}$ ), 7.52 (1H, d,  $J=1.6\text{Hz}$ ),  
7.40 (1H, d,  $J=1.4\text{Hz}$ ), 7.31 (1H, d,  $J=1.4\text{Hz}$ ), 7.13 (1H, dd,  $J=1.6, 8.6\text{Hz}$ ), 5.95 (2H, s),  
4.32 (2H, s), 3.72 (3H, s), 3.67 (2H, t,  $J=8.0\text{Hz}$ ), 1.00 (2H, t,  $J=8.0\text{Hz}$ ), 0.02 (9H, s).

##### STEP 2. Methyl [5-Chloro-2-(imidazole-2-carbonyl)-1H-indol-3-yl]acetate

30 The title compound was prepared according to the procedure described in step 2 of Example 245 from methyl [6-chloro-2-[1-[2-(trimethylsilyl)ethoxymethyl]imidazole-2-carbonyl]-1H-indol-3-yl]acetate (step 1).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.50 (1H, br s), 7.68-7.48 (2H, m), 7.40-7.30 (1H, m), 7.19-7.06 (1H, m), 6.97-6.92 (1H, m), 4.30 (2H, s), 3.67 (3H, s).

#### EXAMPLE 248

##### [6-CHLORO-2-(IMIDAZOLE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

5 The title compound was prepared according to the procedure described in Example 58 from methyl [6-chloro-2-(imidazole-2-carbonyl)-1H-indol-3-yl]acetate (Example 247).

m.p.: 252-253 °C.

10 <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 13.63 (1H, br s), 12.40-12.15 (2H, br), 7.88 (1H, d, J=1.8Hz), 7.78 (1H, d, J=8.6Hz), 7.59 (1H, s), 7.40 (1H, s), 7.11 (1H dd, J=1.8, 8.6Hz), 4.18 (2H, s),

#### EXAMPLE 249

##### METHYL [5-CHLORO-2-(4-METHYLTHIAZOLE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE

15 The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-chloro-2-(phenylsulfonylamino)cinnamate (Example 36, step 3) and 2-bromoacetyl-4-methylthiazole hydrobromide (Cowden, William B. et al., *Aust. J. Chem.*, 1985, 38, 1257).

19 <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.02 (1H, br s), 7.93-7.85 (2H, m), 7.75 (1H, d, J=8.9Hz), 7.38 (1H, dd, J=2.0, 8.9Hz), 4.23 (2H, s), 3.60 (3H, s), 2.61 (3H, s).

#### EXAMPLE 250

##### [5-CHLORO-2-(4-METHYLTHIAZOLE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

25 The title compound was prepared according to the procedure described in Example 58 from methyl [5-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate (Example 249).

m.p.: 218-220 °C.

29 <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.97 (1H, br s), 7.89 (1H, d, J=2.0Hz), 7.75 (1H, d, J=8.7Hz), 7.37 (1H, dd, J=2.0, 8.7Hz), 4.13 (2H, s), 2.62 (3H, s).

30 **EXAMPLE 251**

METHYL [5-CHLORO-2-(1-METHYLPYRROLE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in Example 8 (Method B) from methyl *trans*-5-chloro-2-(phenylsulfonylamino)cinnamate (Example 36, step 3) and 2-chloroacetyl-1-methylpyrrole (P. D. Croce et al., *Synthesis*, 1990, 212).

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.8 (1H, br s), 7.80 (1H, br s), 7.55 (1H, d, J=8.6Hz), 7.40-7.32 (2H, m), 6.95-6.90 (1H, m), 6.35-6.26 (1H, m), 4.00 (2H, s), 3.43 (3H, s), 2.50 (3H, s).

10 **EXAMPLE 252**

[5-CHLORO-2-(1-METHYLPYRROLE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID

A mixture of methyl [5-chloro-2-(1-methylpyrrole-2-carbonyl)-1H-indol-3-yl]acetate (Example 251, 250 mg, 0.79 mmol) and potassium carbonate (900 mg, 6.4 mmol) in methanol-water (1:1, 40 ml) was heated at reflux temperature for 1 h. After cooling to room temperature, the mixture was concentrated. The residue was neutralized with 2N aqueous HCl and extracted with ethyl acetate (50 ml x 2). The combined extracts were dried (MgSO<sub>4</sub>) and concentrated. The residual solids were recrystallized from ethyl acetate/hexane to afford 40 mg (23%) of the title compound as pale yellow solids.

mp: 203-205°C.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.56 (1H, br s), 7.57 (1H, s), 7.33 (1H, d, J=8.6Hz), 7.20-7.10 (2H, m), 6.72 (1H, s), 6.10 (1H, s), 3.81 (2H, s), 2.52 (3H, s).

**EXAMPLE 253**

25 METHYL [5-CHLORO-2-(2-METHYLMIDAZOLE-4-CARBONYL)-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in Example 8 (Method B) from methyl *trans*-5-chloro-2-(phenylsulfonylamino)cinnamate (Example 36, step 3) and 4-bromoacetyl-2-methylimidazole (Deady, Leslie W. et al., *Aust. J. Chem.*, 1981, 34, 1295).

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.04 (1H br s), 8.51 (1H, s), 7.86 (1H, d, J=2.0Hz), 7.71 (1H, d, J=8.9Hz), 7.34 (1H, dd, J=2.0, 8.9Hz), 4.17 (2H, s), 3.59 (3H, s), 2.71 (3H, s).

**EXAMPLE 254**

**[5-CHLORO-2-(2-METHYLMIDAZOLE-4-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

5      The title compound was prepared according to the procedure described in Example 58 from methyl [5-chloro-2-(2-methylimidazole-4-carbonyl)-1H-indol-3-yl]acetate (Example 253).  
m.p.: 237-238 °C.

10     <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.03 (1H, br), 12.00 (1H, s), 8.49 (1H, s), 7.83 (1H, d, J=2.0Hz), 7.70 (1H, d, J=8.9Hz), 7.34 (1H, dd, J=2.0, 8.9Hz), 4.09 (2H, s), 2.87 (3H, s).

**EXAMPLE 255**

**METHYL [5-CHLORO-2-(THIAZOLE-5-CARBONYL)-1H-INDOL-3-YL]ACETATE**

15     The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-chloro-2-(phenylsulfonylamino)cinnamate (Example 36, step 3) and 5-bromoacetylthiazole hydrobromide\*.  
\*5-bromoacetylthiazole hydrobromide was prepared from 5-acetylthiazole according to the procedure for preparing 2-bromoacetyl-4-methylpyridine hydrobromide described in step 2 of Example 31.

1     <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.05 (1H, br s), 9.51 (1H, s), 8.62 (1H, s), 7.85 (1H, d, J=1.9Hz), 7.55 (1H, d, J=8.7Hz), 7.35 (1H, dd, J=1.9, 8.7Hz), 4.09 (2H, s), 3.59 (3H, s).

25     The title compound was prepared according to the procedure described in Example 58 from methyl [5-chloro-2-(thiazole-5-carbonyl)-1H-indol-3-yl]acetate (Example 255).  
m.p.: 175-180 °C.

30     **EXAMPLE 256**

**[5-CHLORO-2-(THIAZOLE-5-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 58 from methyl [5-chloro-2-(thiazole-5-carbonyl)-1H-indol-3-yl]acetate (Example 255).

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.80 (1H, br s), 9.48 (1H, s), 8.74 (1H, s), 7.78 (1H, s), 7.48 (1H, d, J=8.7Hz), 7.30 (1H, d, J=8.9Hz), 3.81 (2H, s).

**EXAMPLE 257**

**METHYL [6-CHLORO-2-(4-METHYLTHIAZOLE-2-CARBONYL)-1H-INDOL-3-**

**5    YL]ACETATE**

The title compound was prepared according to the procedure described in Example 8 (Method B) from methyl *trans*-4-chloro-2-(phenylsulfonylamino)cinnamate (Step 1 of Example 8, Method A) and 2-bromoacetyl-4-methylthiazole hydrobromide (Cowden, William B. et al., *Aust. J. Chem.*, **1985**, 38, 10 1257).

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.95 (1H, br s), 7.90 (1H, s), 7.84 (1H, d, J=8.7Hz), 7.84 (1H, d, J=2.0Hz), 7.15 (1H, d, J=2.0Hz), 4.24 (2H, s), 3.60 (3H, s), 2.62 (3H, s).

**EXAMPLE 258**

**[6-CHLORO-2-(4-METHYLTHIAZOLE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC**

**15    ACID**

The title compound was prepared according to the procedure described in Example 58 from methyl [6-chloro-2-(4methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate (Example 257).

m.p.: 239-240 °C.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.80 (1H, br s), 7.75 (1H, s), 7.68 (1H, d, J=8.4Hz), 7.67 (1H, d, J=2.0Hz), 7.02 (1H, dd, J=2.0, 8.4Hz), 4.03 (2H, s), 2.49 (3H, s).

**EXAMPLE 259**

**METHYL [5-CHLORO-2-[3-(ETHOXYSARONYL)ISOXAZOLE-5-CARBONYL]-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in Example 8 (Method B) from methyl *trans*-5-chloro-2-(phenylsulfonylamino)cinnamate (Example 36, step 3) and ethyl 5-(bromoacetyl)isoxazole-3-carboxylate.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.07 (1H, br s), 7.93 (1H, d, J=1.9Hz), 7.70 (1H, s), 7.39 (1H, dd, J=1.9, 12.8Hz), 7.62 (1H, d, J=12.8Hz), 4.44 (2H, q, J=7.1Hz), 4.15 (2H, s), 3.60 (3H, s), 1.37 (3H, t, J=7.1Hz).

**EXAMPLE 260****[5-CHLORO-2-[3-(CARBOXY)ISOXAZOLE-5-CARBONYL]-1H-INDOL-3-YL]ACETIC ACID**

To a solution of methyl [5-chloro-2-[3-(ethoxycarbonyl)isoxazole-5-carbonyl]-1H-indol-3-yl]acetate (Example 259, 314 mg, 0.80 mmol) in acetic acid (20 ml) was added 2N aqueous HCl (6.0 ml) and the mixture was heated at 110 °C for 5 h. The mixture was then cooled to room temperature and concentrated. The residual yellow solids were washed with ethyl acetate and recrystallized from ethyl acetate/hexane to afford 120 mg (43 %) of the title compound as pale yellow solids.

10 m.p.: 200-205°C.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.01 (1H, s), 7.91 (1H, s), 7.65-7.56 (2H, m), 7.39 (1H, d, J=8.9Hz), 4.06 (2H, s).

**EXAMPLE 261****METHYL [6-CHLORO-2-CYCLOPROPANE CARBONYL-1H-INDOL-3-YL]ACETATE**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and bromomethyl cyclopropyl ketone\* .

15 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.55 (1H, br s), 7.58 (1H, d, J=8.56Hz), 7.26 (1H, d, J=1.97Hz), 7.10 (1H, dd, J=8.56Hz, 1.97Hz), 4.17 (2H, s), 3.73 (3H, s), 2.58-2.49 (1H,m), 1.80-1.78 (2H, m), 1.09-1.02 (2H, m).

\*Bromomethylcyclopropyl ketone was prepared from cyclopropyl methyl ketone according to the procedure for preparing 4-(trifluoromethoxy)phenacyl bromide described in Example 189.

20 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 3.91 (2H, s), 2.65 (1H, t, 6.94Hz), 1.20-0.98 (4H, m).

**EXAMPLE 262****[6-CHLORO-2-CYCLOPROPANE CARBONYL-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl 2-(6-chloro-2-cyclopropanecarbonyl-1H-indol-3-yl)acetate (Example 261).

30 m.p.: 207-210 °C.

IR (KBr) v: 3304, 3013, 1709, 1624, 1566, 1443, 1414, 1387, 1340, 1286, 1248, 1217, 1200, 1157, 1057, 1045, 1022 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.98 (1H, br s), 7.75 (1H, d, J=8.75Hz), 7.48 (1H, d, J=1.81Hz) 7.11 (1H, dd, J=8.75Hz, 1.81Hz), 4.08 (2H, s), 2.73 (1H, quintet, 6.24Hz), 1.07 (4H, d, 6.24Hz).

#### EXAMPLE 263

##### METHYL [6-CHLORO-2-CYCLOBUTANECARBONYL-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of Example 8, Method A) and bromomethyl cyclobutyl ketone\*.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.35 (1H, br s), 7.53 (1H, d, J=8.72Hz), 7.18 (1H, d, J=1.65Hz) 7.07 (1H, dd, J=8.72Hz, 1.65Hz), 4.10 (2H, s), 3.77 (3H, s), 3.72 (1H, m), 2.44-1.86 (6H, m).

\*Bromomethylcyclobutyl ketone was prepared from cyclobutyl methyl ketone according to the procedure for preparing 4-(trifluoromethoxy)phenacyl bromide described in Example 189.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 3.88 (2H, s), 3.60 (1H, m), 2.33-1.80 (6H, m)

#### EXAMPLE 264

##### [6-CHLORO-2-CYCLOBUTANECARBONYL-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl 2-(6-chloro-2-cyclobutanecarbonyl-1H-indol-3-yl)acetate (Example 263).

m.p.: 225-228 °C.

IR (KBr) v: 3303, 2954, 1705, 1632, 1564, 1529, 1437, 1412, 1335, 1242, 1213, 1188, 1157, 1056, 1024 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.63 (1H, br s), 7.71 (1H, d, J=8.72Hz), 7.46 (1H, d, J=1.81Hz), 7.09 (1H, dd, J=8.72Hz, 1.81Hz), 4.04 (2H, s), 2.30-1.78(7H, m).

#### EXAMPLE 265

##### METHYL [5-(*tert*-BUTYL)-2-(4-CHLOROBENZOYL)-1H-INDOL-3-YL]ACETATE

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-*tert*-butyl-2-(*p*-toluenesulfonylamino)cinnamate (Example 143, step 2) and 4-chlorophenacyl bromide.

5     <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.82 (1H, br s), 7.8-7.31 (7H, m), 3.87 (2H, s), 3.67 (3H, s), 1.38 (9H, s).

#### EXAMPLE 266

##### [5-(*tert*-BUTYL)-2-(4-CHLOROBENZOYL)-1H-INDOL-3-YL] ACETIC ACID

The title compound was prepared according to the procedure described in 10 Example 9 (Method B) from methyl [5-*tert*-butyl-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetate (Example 265).

m.p.: 171°C.

IR (KBr) v: 3241, 2963, 1699, 1634, 1589/ 1541, 1394, 1331, 1222, 1091, 1011 cm<sup>-1</sup>.

15     <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.48 (1H, br s), 7.78-7.37 (7H, m), 3.85 (2H, s), 1.34 (9H, s)

#### EXAMPLE 267

##### [6-CHLORO-2-(4-METHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]-N,N-DIMETHYLACETAMIDE

The title compound was prepared according to the procedure described in 20 Example 43 from [6-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid (Example 31).

m.p.: 208 °C (decompose).

IR (KBr): 3233, 1655, 1638, 1524, 1398, 1200, 1134 cm<sup>-1</sup>.

18     <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.54 (1H, br s), 8.62 (1H, d, J=5.0Hz), 8.15 (1H, br), 7.79 (1H, d, J=8.7Hz), 7.49 (1H, d, J=1.8Hz), 7.40-7.30 (1H, m), 7.09 (1H, dd, J=1.8, 8.7Hz), 4.43 (2H, s), 3.16 (3H, s), 2.98 (3H, s), 2.48 (3H, s).

#### EXAMPLE 268

##### [6-CHLORO-2-(4-METHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]-N-METHYLACETAMIDE

The title compound was prepared according to the procedure described in 30 Example 43 from [6-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid (Example 31) and methylamine hydrochloride.

m.p.: 231 °C.

IR (KBr)  $\nu$ : 3306, 1643, 1595, 1560, 1526, 1277, 1202, 797 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 12.45 (1H, br), 8.64 (1H, d, J=4.9Hz), 8.19 (1H, br), 7.85 (1H, d, J=8.6Hz), 7.50 (1H, br), 7.40 (1H, br d, J=4.6Hz), 7.15 (1H, dd, J=1.6, 8.9Hz), 6.67 (1H, br), 4.14 (2H, s), 2.73 (3H, d, J=4.8Hz), 2.51 (3H, s).

**EXAMPLE 269**

**[5-CHLORO-2-(4-METHYL PYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]-N-(2-HYDROXYETHYL)ACETAMIDE**

The title compound was prepared according to the procedure described in Example 43 from [5-chloro-2-(4-methylpyridine)-1H-indol-3-yl]acetic acid (Example 36) and 2-aminoethanol.

MS (EI) m/z: 371 (M<sup>+</sup>).

m.p.: 195.9 °C.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 12.28 (1H, br s), 8.69 (1H, d, J=4.9Hz), 7.94 (1H, br s), 7.78 (2H, m), 7.66 (1H, d, J=8.7Hz), 7.56 (1H, m), 7.31 (1H, dd, J=2.0Hz, 8.7Hz), 3.94 (2H, s), 3.09 (2H, dd, J=5.93Hz, 11.86Hz), 2.47 (3H, s).

**EXAMPLE 270**

**[5-CHLORO-2-(4-METHYL PYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]-N-METHOXYACETAMIDE**

The title compound was prepared according to the procedure described in Example 43 from [5-chloro-2-(4-methylpyridine)-1H-indol-3-yl]acetic acid (Example 36) and *O*-methylhydroxylamine hydrochloride.

MS (EI) m/z: 357 (M<sup>+</sup>).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 12.53 (1H, br s), 9.54 (1H, br s), 8.65 (1H, d, J=5.1Hz), 8.19 (1H, br s), 7.92 (1H, br s), 7.42 (2H, m), 7.34 (1H, dd, J=1.7Hz, 8.9Hz), 4.01 (2H, s), 3.74 (3H, s), 2.52 (3H, s).

**EXAMPLE 271**

**2-[5-CHLORO-2-(4-METHYL PYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]-1-(1-PIPERAZINYL)-1-ETHANONE**

30 STEP 1. **2-[5-Chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]-1-(4-tert-butoxycarbonyl-1-piperazinyl)-1-ethanone**

The title compound was prepared according to the procedure described in Example 43 from [5-chloro-2-(4-methylpyridine)-1H-indol-3-yl]acetic acid (Example 36) and *tert*-butyl 1-piperadinecarboxylate.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.61 (1H, br s), 8.62 (1H, d, J=5.1Hz), 8.14 (1H, br s), 7.84 (1H, s), 7.42 (1H, d, J=8.7Hz), 7.37 (br d, 1H, J=4.9Hz), 7.30 (1H, dd, J=2.0Hz, 8.9Hz), 4.42 (2H, s), 3.66 (4H, m), 2.50 (3H, s), 1.64 (4H, m), 1.46 (9H, s).

**STEP2. 2-[5-Chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]-1-(1-piperazinyl)-1-ethanone**

To a solution of [5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]-N-(4-*tert*-butoxycarbonylpiperadino)acetamide (step 1, 152.6 mg, 0.042 mmol) in THF (1 ml) was added dropwise trifluoroacetic acid (2 ml) at 0°C. The mixture was stirred at room temperature for 1.5h and then concentrated. The residue was diluted with dichloromethane (25 ml), washed with saturated aqueous sodium bicarbonate (25 ml). The aqueous layer was extracted with dichloromethane (25 ml x 2). The combined organic layers were dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated. The residue was purified by flash column chromatography on eluting with methanol/dichloromethane (1:10) to afford 80.8 mg of the title compound as yellow crystals.

MS (EI) m/z: 396(M<sup>+</sup>).

m.p.: 205.0 °C.

IR (KBr) ν : 3244, 1647, 1595, 1525, 1429, 1205 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.28 (1H, br s), 8.68 (1H, d, J=4.9Hz), 7.90 (1H, br s), 7.81 (1H, br s), 7.65 (1H, d, J=8.9Hz), 7.56 (br d, 1H, J=4.1Hz), 7.31 (1H, dd, J=1.8Hz, 8.9Hz), 4.15 (2H, br s), 3.50-3.15 (4H, m), 2.70-2.55 (4H, m), 2.46 (3H, s).

**EXAMPLE 272**

**25 [5-CHLORO-2-(4-METHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]-N-(2-AMINOETHYL)ACETAMIDE**

**STEP 1. [5-Chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]-N-(2-*tert*-butoxycarbonylaminoethyl)acetamide**

The title compound was prepared according to the procedure described in Example 43 from [5-chloro-2-(4-methylpyridine)-1H-indol-3-yl]acetic acid (Example 36) and *N*-(2-aminoethyl)carbamic acid *tert*-butyl ester.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.29 (1H, br s), 8.68 (1H, d, J=4.9Hz), 7.94 (1H, br s), 7.78 (2H, m), 7.67 (1H, d, J=8.9Hz), 7.57 (1H, br d, J=4.9Hz), 7.32 (dd, 1H, J=2.0Hz, 8.7Hz), 6.73 (1H, m), 3.94 (2H, s), 3.05-2.95 (4H, m), 2.47 (3H, s), 1.35 (9H, s).

STEP2.[5-Chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]-N-(2-

5 aminoethyl)acetamide

The title compound was prepared according to the procedure described in step 2 of Example 273 from [5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]-N-(2-*tert*-butoxycarbonylaminoethyl)acetamide (step 1).

MS (EI) m/z: 370 (M<sup>+</sup>).

10 m.p.: 165.7 °C.

IR (KBr) ν : 3346, 2927, 1665, 1627, 1593, 1515, 1435, 1267, 1207 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.28 (1H, br s), 8.69 (1H, d, J=4.9Hz), 7.93 (1H, br s), 7.80-7.76 (2H, m), 7.66 (1H, d, J=8.9Hz), 7.57 (1H, m), 7.31 (dd, 1H, J=2.0Hz, 8.9Hz), 3.94 (2H, s), 3.01 (2H, q, J=5.77Hz), 2.55-2.45 (2H, m), 2.47 (3H, s).

15 **EXAMPLE 273**

2-[5-CHLORO-2-(4-METHYL PYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]-1-(3-AMINO-1-PYRROLIDINYL)-1-ETHANONE

STEP1.2-[5-Chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]-1-[3-(*tert*-butoxycarbonylamino)-1-pyrrolidinyl]-1-ethanone

20 The title compound was prepared according to the procedure described in Example 43 from [5-chloro-2-(4-methylpyridine)-1H-indol-3-yl]acetic acid (Example 36) and 3-(*tert*-butoxycarbonylamino)pyrrolidine.

25 <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.56 (1H, br s), 8.62 (1H, d, J=4.9Hz), 8.18 (1H, br s), 7.78 (1H, br s), 7.42 (1H, d, J=8.9Hz), 7.35 (1H, br d, J=4.9Hz), 7.29 (2H,m), 4.89 (1H, br d, J=25.05), 4.36-3.45 (7H, m), 2.48 (3H, s), 2.35-1.80 (2H, m), 1.46 (9H, s).

STEP2.2-[5-Chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]-1-(3-amino-1-pyrrolidinyl)-1-ethanone

30 The title compound was prepared according to the procedure described in step 2 of Example 271 from 2-[5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]-1-[3-(*tert*-butoxycarbonylamino)-1-pyrrolidinyl]-1-ethanone (step 1).

MS (EI) m/z: 396(M<sup>+</sup>).

m.p.: 179.2 °C.

IR (KBr)  $\nu$  : 3238, 2876, 1638, 1595, 1526, 1423, 1203  $\text{cm}^{-1}$

$^1\text{H-NMR}$  (DMSO-d<sub>6</sub>)  $\delta$ : 12.26 (1H, br s), 8.68 (1H, d, J=4.9Hz), 7.89 (1H, br s), 7.81 (1H, d, J=1.81Hz), 7.65 (1H, d, J=8.9Hz), 7.55 (1H, br d, J=5.1Hz), 7.31 (dd, 1H, J=2.0Hz, 8.7Hz), 4.07 (1H, s), 4.05 (1H, s), 3.70-2.90 (5H, m), 2.46 (3H, s), 2.10-1.80 (1H, m), 1.75-1.45 (1H, m).

**EXAMPLE 274**

METHYL [6-CHLORO-2-(4-CHLOROBENZOYL)-5-FLUORO-1H-INDOL-3-YL]ACETATE

10 **STEP 1. Methyl trans-2-amino-4-chloro-5-fluorocinnamate**

The title compound was prepared according to the procedure described in step 1 of Example 133 from 2-bromo-5-chloro-4-fluoroaniline (JP 01311056 A2, Nippon Kayaku Co., Ltd., Japan).

15  $^1\text{H-NMR}$  (CDCl<sub>3</sub>)  $\delta$ : 7.69 (1H, d, J=15.8Hz), 7.15 (1H, d, J=9.7Hz), 6.74 (1H, d, J=6.4Hz), 6.31 (1H, d, J=15.8Hz), 3.81 (3H, s).

**STEP 2. Methyl trans-4-chloro-5-fluoro-2-(phenylsulfonylamino)cinnamate**

The title compound was prepared according to the procedure described in step 1 of Example 8 (Method A) from methyl *trans*-2-amino-4-chloro-5-fluorocinnamate (step 1).

20  $^1\text{H-NMR}$  (CDCl<sub>3</sub>)  $\delta$ : 7.71-7.68 (1H, m), 7.57-7.40 (6H, m), 7.23 (1H, d, J=9.4Hz), 6.09 (1H, d, J=15.8Hz), 3.77 (3H, s).

**STEP 3. Methyl [6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetate**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-chloro-5-fluoro-2-(phenylsulfonylamino)cinnamate (step 2).

25  $^1\text{H-NMR}$  (CDCl<sub>3</sub>)  $\delta$ : 9.05 (1H, br.s), 7.74 (2H, d, J=8.7Hz), 7.49 (2H, d, J=8.7Hz), 7.35-7.32 (2H, m), 3.77 (2H, s), 3.66 (3H, s)

**EXAMPLE 275**

[6-CHLORO-2-(4-CHLOROBENZOYL)-5-FLUORO-1H-INDOL-3-YL]ACETIC

30 **ACID**

The title compound was prepared according to the procedure described in Example 58 from methyl [6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetate. m.p.: 215-220 °C.

IR(KBr)v: 1709, 1626, 1585, 1529, 1456, 1439, 1279, 1250 cm<sup>-1</sup>.

- 5   <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.85 (1H, br.s), 7.79-7.75 (3H, m), 7.67-7.63 (2H, m), 7.60-7.58 (1H, m), 3.83 (2H, s).

**EXAMPLE 276**

**METHYL [6-CHLORO-5-FLUORO-2-(4-METHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE**

10   The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-chloro-5-fluoro-2-(phenylsulfonylamino)cinnamate (Example 274, step 2).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.54 (1H, br.s), 8.58 (1H, d, J=4.9Hz), 8.14 (1H, m), 7.56-7.53 (1H, m), 7.39-7.34 (2H, m), 4.25 (2H, s), 3.75 (3H, s), 2.48 (3H, s).

15   **EXAMPLE 277**

**[6-CHLORO-5-FLUORO-2-(4-METHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

20   The title compound was prepared according to the procedure described in Example 58 from methyl [6-chloro-5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 276).

mp: 219.5 °C.

IR (KBr) v: 1732, 1709, 1647, 1597, 1529, 1279, 1252, 1204 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.35 (1H, br.s), 8.70 (1H, d, J=5.1Hz), 7.96 (1H, s), 7.87 (1H, d, J=6.6Hz), 7.81 (1H, d, J=10.1Hz), 7.59-7.58 (1H, m), 4.05 (2H, s), 2.47 (3H, s).

25   **EXAMPLE 278**

**METHYL [6-CHLORO-2-[4-(1-HYDROXYETHYL)PYRIDINE-2-CARBONYL]-1H-INDOL-3-YL]ACETATE**

**STEP 1. methyl [6-chloro-2-[4-[1-(*tert*-butyldimethylsilyloxy)ethyl]pyridine-2-carbonyl]-1H-indol-3-yl]acetate**

30   The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-chloro-2-(phenylsulfonylamino)cinnamate (step 1 of

Example 8, Method A) and 2-bromoacetyl-4-[1-(*tert*-butyldimethylsilyloxy)ethyl]pyridine\*.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.49 (1H, br s), 8.71 (1H, d, J=4.9Hz), 8.24 (1H, d, J=1.5Hz), 7.61-7.63 (2H, m), 7.53 (1H, d, J=1.8Hz), 7.13 (1H, dd, J=1.8, 8.7Hz), 4.96 (1H, q, J=6.4Hz), 4.32 (2H, s), 3.73 (3H, s), 1.45 (3H, d, J=6.4Hz), 0.93 (9H, s), 0.10 (3H, s), 0.03 (3H, s).

\*2-Bromoacetyl-4-[1-(*tert*-butyldimethylsilyloxy)ethyl]pyridine was prepared as follows;

4-[1-(Trimethylsilyloxy)ethyl]-2-pyridinecarbonitrile:

10 The title compound was prepared from 4-(1-hydroxyethyl)pyridine-N-oxide (C.W.Muth et al., *J. Heterocycl. Chem.*, 1972, 9, 1299) according to the procedure for preparing 4-chloro-2-pyridinecarbonitrile described in Example 33.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.64 (1H, d, J=5.1Hz), 7.69-7.70 (1H, m), 7.45-7.48 (1H, m), 4.88 (2H, q, J=6.4Hz), 1.43 (3H, d, J=6.6Hz), 0.14 (9H, s).

15 4-[1-(*tert*-Butyldimethylsilyloxy)ethyl]-2-pyridinecarbonitrile:

To a solution of 4-[1-(trimethylsilyloxy)ethyl]-2-pyridinecarbonitrile (39.04 g, 0.1624 mol) in THF (200 ml) was added a solution of tetrabutylammonium fluoride in THF (1M, 178.6 ml, 0.1786 mol) at room temperature. After stirring for 0.5 h, the mixture was concentrated. The residue was diluted with ethyl acetate (300 ml) and washed with water (200 ml). The aqueous layer was then extracted with dichloromethane (200 ml x 2). The combined organic layers were dried (MgSO<sub>4</sub>) and concentrated. The residual oil was dissolved in DMF (200 ml). To the solution was added *tert*-butyldimethylsilylchloride (36.72 g, 0.2436 mol) and imidazole (22.11 g, 0.3248 mol) at room temperature. After stirring for 19h, diethyl ether (500 ml) and water (200 ml) were added to the mixture and the organic layer was separated. The organic layer was washed with water (100 ml x 2), dried (MgSO<sub>4</sub>) and concentrated. The residue was purified by flash column chromatography eluting with ethyl acetate/hexane (1:20) to give 39.23 g (92 %) of the title compound as an oil.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.64 (1H, d, J=5.1Hz), 7.67-7.68 (1H, m), 7.46-7.48 (1H, m), 4.89 (1H, q, J=6.4Hz), 1.42 (3H, d, J=6.4Hz), 0.92 (9H, s), 0.10 (6H, s).

**2-Acetyl-4-[1-(*tert*-butyldimethylsilyloxy)ethyl]pyridine:**

The title compound was prepared from 4-[1-(*tert*-butyldimethylsilyloxy)ethyl]-2-pyridinecarbonitrile according to the procedure for preparing 2-acetyl-4-chloropyridine described Example 33.

5       $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.62 (1H, d,  $J=4.9\text{Hz}$ ), 7.95-7.96 (1H, m), 7.49-7.52 (1H, m), 4.91 (1H, q,  $J=6.4\text{Hz}$ ), 2.73 (3H, s), 1.41 (3H, d,  $J=6.4\text{Hz}$ ), 0.91 (9H, s), 0.10 (6H, s).

**2-Bromoacetyl-4-[1-(*tert*-butyldimethylsilyloxy)ethyl]pyridine**

The title compound was prepared according to the procedure for preparing 2-bromoacetyl-4-(*tert*-butyldimethylsilyloxymethyl)pyridine described in Example 95  
10 from 2-acetyl-4-[1-(*tert*-butyldimethylsilyloxy)ethyl]pyridine.

**STEP 2. Methyl [6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate.**

The title compound was prepared according to the procedure described in step  
2 of Example 95 from methyl [6-chloro-2-[4-[1-(*tert*-butyldimethylsilyloxy)ethyl]pyridine-2-carbonyl]-1H-indol-3-yl]acetate (step 1).  
15

1       $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$ : 12.34 (1H, br s), 8.77 (1H, d,  $J=5.1\text{Hz}$ ), 8.11 (1H, s), 7.81 (1H, d,  $J=8.7\text{Hz}$ ), 7.75 (1H, d,  $J=1.6\text{Hz}$ ), 7.70 (1H, dd,  $J=1.2, 4.9\text{Hz}$ ), 7.13 (1H, dd,  $J=1.8, 8.6\text{Hz}$ ), 5.61 (1H, d,  $J=4.6\text{Hz}$ ), 4.84-4.93 (1H, m), 4.17 (2H, s), 3.59 (3H, s), 1.39 (3H, d,  $J=6.4\text{Hz}$ ).

**20      EXAMPLE 279****[6-CHLORO-2-[4-(1-HYDROXYETHYL)PYRIDINE-2-CARBONYL]-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 58 from methyl [6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate (Example 278).  
25

m.p.: 193-194°C.

IR (KBr)  $\nu$ : 3464, 1707, 1632, 1591, 1526, 1250, 1225, 1192, 1144, 914  $\text{cm}^{-1}$ .

1       $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$ : 12.30 (1H, br s), 8.78 (1H, d,  $J=5.1\text{Hz}$ ), 8.11 (1H, s), 7.79 (1H, d,  $J=8.6\text{Hz}$ ), 7.74 (1H, d,  $J=1.6\text{Hz}$ ), 7.71 (1H, d,  $J=5.3\text{Hz}$ ), 7.12 (1H, dd,  $J=1.8, 8.7\text{Hz}$ ),

30      5.60 (1H, d,  $J=4.4\text{Hz}$ ), 4.84-4.93 (1H, m), 4.09 (2H, s), 1.39 (3H, d,  $J=6.6\text{Hz}$ ).

**EXAMPLE 280****[6-CHLORO-2-(4-ETHYL-3-FLUOROPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in  
5 Example 112 from methyl [6-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetate (Example 113).  
m.p.; 193-194°C.

IR (KBr)  $\nu$ : 3256, 1707, 1645, 1529, 1420, 1227, 1180, 1159, 1153  $\text{cm}^{-1}$ .

MS (EI) m/z: 360 ( $M^+$ ).

10  $^1\text{H-NMR}$  (DMSO-d<sub>6</sub>)  $\delta$ : 11.84 (1H, br s), 8.46 (1H, d, J=5.3Hz), 7.77 (1H, d, J=8.7Hz),  
7.67 (1H, t, J=5.1Hz), 7.51 (1H, d, J=1.8Hz), 7.12 (1H, dd, J=1.8, 8.6Hz), 3.74 (2H, s),  
2.76 (2H, q, J=7.6Hz), 1.25 (3H, t, J=7.6Hz).

**EXAMPLE 281****[6-CHLORO-2-(2-NITROBENZOYL)-1H-INDOL-3-YL]ACETIC ACID****15 STEP 1. Polymer-bound *trans* 4-chloro-2-(phenylsulfonylamino)cinnamate**

To a mixture of Wang resin (200-400 mesh, 1.37 g, ca. 0.89 mmol) and *trans*-4-chloro-2-(phenylsulfonylamino)cinnamic acid (600 mg, 1.77 mmol) was added dichloromethane (10 ml) and *N,N*-diisopropylethylamine (1.86 ml, 10.7 mmol). The mixture was allowed to stand for 1h, and then 4-dimethylaminopyridine (22 mg, 0.18 mmol) and WSC (339 mg, 1.77 mmol) were added. The mixture was agitated for 18h and filtrated. The residual resin was washed with water (20 ml x 3), methanol (20 ml x 3), acetone (20 ml x 3), dichloromethane (20 ml x 3) and dried to give 1.65 g of the title compound.

**STEP 2. [6-chloro-2-(2-nitrobenzoyl)-1H-indol-3-yl]acetic acid**

25 To a mixture of polymer-bound *trans*-4-chloro-2-(phenylsulfonylamino)cinnamate (step 1, 100mg, 53  $\mu\text{mol}$ ) and 2-nitrophenacyl bromide (39 mg, 0.16 mmol) in acetone (3 ml) was added potassium carbonate (37 mg, 0.27 mmol). The mixture was agitated for 18 h. and filtrated. The residual resin was washed with water (20 ml x 3), acetone (20ml x 3), dichloromethane (20 ml x 3) and  
30 THF (20 ml x 2) and dried. The resin was diluted with THF (4 ml) and then DBU was added (40 $\mu\text{l}$ , 0.27mmol). After agitating for 6 h, the resin was filtered off and

washed with THF (20 ml x 3), acetone (20 ml x 3) and dichloromethane (20 ml x 3). To the resin was added 95% trifluoroacetic acid in dichloromethane (5 ml) and the mixture was agitated for 3h. The mixture was filtered and the residue was washed with dichloromethane (20ml x 5). The filtrate was concentrated and the residue was  
5 purified by HPLC (MeOH/AcONH<sub>4</sub> aqueous solution=60/40-90/10) to give 3.2 mg (17%) of the title compound.

MS (ESI) m/z : 359 (MH<sup>+</sup>).

#### EXAMPLE 282

##### [6-CHLORO-2-(2,4-DIMETHOXYBENZOYL)-1H-INDOL-3-YL]ACETIC ACID

10 The title compound was prepared according to the procedure described in Example 281 from 4-chloro-2-(phenylsulfonylamino)cinnamic acid.

MS (ESI) m/z : 374 (MH<sup>+</sup>).

#### EXAMPLE 283

##### [6-CHLORO-2-(4-DIFLUOROMETHOXYBENZOYL)-1H-INDOL-3-YL]ACETIC 15 ACID

The title compound was prepared according to the procedure described in Example 289 from 4-chloro-2-(phenylsulfonylamino)cinnamic acid.

MS (ESI) m/z : 380 (MH<sup>+</sup>).

#### EXAMPLE 284

##### [6-CHLORO-2-(2,5-DIMETHOXYBENZOYL)-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in Example 281 from 4-chloro-2-(phenylsulfonylamino)cinnamic acid.

MS (ESI) m/z : 374 (MH<sup>+</sup>).

#### EXAMPLE 285

##### METHYL [5-ACETYL-2-(4-CHLOROBENZOYL)-1H-INDOL-3-YL]ACETATE

###### STEP 1. 4-ACETYL-2-BROMOANILINE

To a stirred suspension of 4-acetamido-3-bromoacetophenone in ethanol (12 ml) was added dropwise hydrochloric acid (3 ml) at 0 °C. The reaction mixture was stirred under reflux condition for 4.5 h. The mixture was cooled and concentrated.  
30 The residual solids were partitioned between saturated aqueous sodium bicarbonate (50 ml) and diethyl ether (50 ml). The aqueous layer was extracted with ethyl acetate (50

ml x 2). The combined organic layers were dried ( $\text{MgSO}_4$ ) and concentrated to afford 1.79g (quant.) of the title compound as a brown oil.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.06 (1H, d, 1.97Hz), 7.76-7.72 (1H, m), 6.74 (1H, d, 8.40Hz), 4.60 (1H, br s), 2.50 (s, 3H)

5 **STEP 2. Methyl *trans*-(5-acetyl-2-amino)cinnamate**

The title compound was prepared according to the procedure described in step 1 of Example 133 from 4-acetyl-2-bromoaniline (step 1) and methyl acrylate.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.02 (1H, d, 2.13Hz), 7.81-7.75 (2H, m), 6.70 (1H, d, 8.56Hz), 6.44 (1H, d, 15.8Hz), 4.55 (2H, br s), 3.81 (3H, s), 2.53 (3H, s).

10 **STEP 3 . Methyl *trans*-5-acetyl-2-(*p*-toluenesulfonylamino)cinnamate**

The title compound was prepared according to the procedure described in step 1 of Example 8 (Method A) from methyl *trans*-(5-acetyl-2-amino)cinnamate (step 2) and *p*-toluenesulfonyl chloride.

15  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.01 (1H, d, 2.00Hz), 7.89 (1H, dd, 8.59Hz, 1.97Hz), 7.68-7.22 (7H, m), 6.30 (1H, s), 6.15 (1H, d, 15.8Hz), 3.81 (3H, s), 2.57 (3H, s), 2.38 (3H, s)

**STEP 4 . Methyl [5-acetyl-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetate**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-5-acetyl-3-(*p*-toluenesulfonylamino)cinnamate (step 3) and 4-chlorophenacyl bromide.

20  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 9.2 (1H, br s), 8.34-7.75 (4H, m), 7.52 - 7.45 (3H, m), 3.89 (2H, s), 3.69 (3H, s), 2.68 (3H, s).

**EXAMPLE 286**

**[5-ACETYL-2-(4-CHLOROBENZOYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Method B of Example 9 from methyl [5-acetyl-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetate (Example 285).

m.p. : 225°C.

IR (KBr) v: 3281, 1703, 1666, 1643, 1614, 1574, 1539, 1452, 1425, 1402, 1364, 1263, 1240, 1178, 1092, 1011, 959  $\text{cm}^{-1}$

30  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$ : 12.01 (1H, br s), 8.49 (1H, br s), 7.93 - 7.89 (1H, m), 7.78 (2H, d, 8.56Hz), 7.65 (d, 2H, 8.56Hz), 7.52 (1H, d, 8.72Hz), 3.93 (2H, s), 2.63 (3H, s).

**EXAMPLE 287****METHYL [6-FLUORO-2-(4-METHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETATE****STEP 1. Methyl *trans*-(4-fluoro-2-nitro)cinnamate**

5       The title compound was prepared according to the procedure described in step 1 of Example 133 from 3-fluoro-6-iodonitrobenzene and methyl acrylate .

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.67 (1H, d, 15.8Hz), 7.78 (1H, dd, 8.07Hz, 2.65Hz), 7.68-7.63 (2H, m), 6.34 (1H, d, 15.8Hz), 3.84 (3H, s).

**STEP 2. Methyl *trans*-(2-amino-4-fluoro)cinnamate**

10      The title compound was prepared according to the procedure described in step 2 of Example 36 from methyl *trans*-(4-fluoro-2-nitro)cinnamate (step 1).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.75 (1H, d, 15.8Hz), 7.37-7.31 (1H, m), 6.50-6.37 (2H, m), 6.32-6.26 (1H, m), 4.13 (2H, br s), 3.80 (3H, s).

**STEP 3. Methyl *trans*-4-fluoro-2-(*p*-toluenesulfonylamino)cinnamate**

15      The title compound was prepared according to the procedure described in step 1 of Example 8 (Method A) from methyl *trans*-(2-amino-4-fluoro)cinnamate (step 2) .

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.64 (1H, d, 8.40Hz), 7.46-7.19 (4H, m), 6.94-6.87 (1H, m), 6.77 (1H, s), 6.16-6.10 (1H, m), 3.79 (3H, s) , 2.38 (3H, s) .

**STEP 4. Methyl [6-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-****yl]acetate**

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-fluoro-2-(*p*-toluenesulfonylamino)cinnamate (step 3).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.49 (1H, br s), 8.61 (1H, d, 4.94Hz), 8.17-7.61 (2H, m), 7.36-7.14 (2H, m), 6.98-6.90 (1H, m), 4.31 (2H, s), 3.73 (3H, s), 2.47 (3H, s).

**25 EXAMPLE 288****[6-FLUORO-2-(4-METHYLPYRIDINE-2-CARBONYL)-1H-INDOL-3-YL]ACETIC ACID**

The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl [6-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-

30      indol-3-yl]acetate (Example 287).

m.p.: 208 °C.

IR (KBr) v: 3238, 1701, 1638, 1597, 1533, 1398, 1281, 1211, 1132, 1003 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.28 (1H, br s), 8.70 (1H, d, 4.94Hz), 7.96 (1H, s), 7.83-7.77 (1H, m), 7.57 (1H, d, 4.94Hz), 7.42 (1H, dd, 10.2Hz, 2.13Hz), 7.03-6.95 (1H, m), 4.09 (2H, s), 2.47 (3H, s).

#### EXAMPLE289

##### METHYL [6-FLUORO-2-(4-CHLOROBENZOYL)-1H-INDOL-3-YL] ACETATE

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-4-fluoro-3-(*p*-toluenesulfonylamino)cinnamate (step 3 of Example 287) and 4-chlorophenacylbromide.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 9.10 (1H, br s), 7.76-7.71 (2H, m), 7.60-7.54 (2H,m), 7.50-7.45 (2H, m), 7.04-6.90 (2H, m), 3.81 (2H, s), 3.66 (3H, s).

#### EXAMPLE290

##### [6-FLUORO-2-(4-CHLOROBENZOYL)-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in Example 9 (Method B) from methyl [6-fluoro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetate (Example 289).

m.p.: 214 °C.

IR(KBr)v: 3335, 1699, 1618, 1605, 1587, 1531, 1425, 1327, 1267, 1231, 1134, 1064, 1001 cm<sup>-1</sup>.

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 11.73 (1H, br s), 7.78-7.63 (5H, m), 7.17 (1H, dd, 9.72Hz, 2.13Hz), 7.04-6.96 (1H, m), 3.84 (2H, s).

#### EXAMPLE 291

##### [2-(4-METHYLPYRIDINE-2-CARBONYL)-5-METHYLTHIO-1H-INDOL-3-YL]ACETIC ACID

###### STEP 1. Methyl *trans*-(2-amino-5-methylthio)cinnamate

The title compound was prepared according to the procedure described in step 1 of Example 133 from 2-bromo-4-methylthioxaniline (JP80-122756) and methyl acrylate.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.77 (1H, d, 15.8Hz), 7.38 (1H, d, 2.13Hz), 7.19 (1H, dd, 8.40Hz, 2.13Hz), 6.66 (1H, d, 8.40Hz), 6.36 (1H, d, 15.8Hz), 3.97 (1H, br s), 3.80 (3H, s), 2.43

(3H, s).

STEP 2 . Methyl *trans*-2-p-toluenesulfonylamino-5-methylthiocinnamate

The title compound was prepared according to the procedure described in step 1 of Example 8 from methyl *trans*-(2-amino-4-methylthio)cinnamate (step 1) and *p*-toluenesulfonyl chloride.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.81 (2H, d, 8.40Hz), 7.56-6.91 (8H, m), 6. 13 (1H, d, 15.6Hz), 3.79 (3H, s), 2.46 (3H, s), 2.39 (3H, s).

STEP 3. Methyl [2-(4-methylpyridine-2-carbonyl)-5-methylthio-1H-indol-3-yl]acetate

The title compound was prepared according to the procedure described in Example 57 from methyl *trans*-2-p-toluenesulfonylamino-5-methylthiocinnamate (step 2) and 2-bromoacetyl-4-methylpyridine hydrobromide (Preparation is described in step 2 of Example 31).

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 12.47 (1H, br s), 8.62 (1H, d, 4.78Hz), 8.19-8.17 (1H, m), 7.65-7.62(1H,m), 7.47-7.30 (3H,m), 4.31 (2H, s), 3.73 (3H, s), 2.48 (3H, s).

**15 EXAMPLE 292**

[2-(4-METHYL PYRIDINE-2-CARBONYL)-5-METHYLTHIO-1H-INDOL-3-YL]ACETIC ACID

The title compound was prepared according to the procedure described in Method B of Example 9 from methyl [2-(4-methylpyridine-2-carbonyl)-5-methylthio-1H-indol-3-yl]acetate (Example ).

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 12.22 (1H, br s), 8.70 (1H, d, 4.62Hz), 7.95-7.17 (4H, m), 4.08 (2H, s), 2.47 (3H, s), 2.35 (3H, s).

MS (EI) m/z: 340 (M<sup>+</sup>).

**Example 293**

**25 3-[4-Chloro-2-(toluene-4-sulfonylamino)-phenyl]-acrylic acid ethyl ester**

To 3-(2-amino-4-chloro-phenyl)-acrylic acid ethyl ester (18.0g, 79.8 mmol) in dichloromethane (144 ml) was added pyridine (9.04 ml, 112 mmol) and *p*-toluenesulfonyl chloride (16.0g, 83.9 mmol). The reaction was stirred at room temperature for 18 hours and poured into 1N hydrochloric acid (150 ml). The layers were separated and the organic layer was dried over magnesium sulfate, filtered, and concentrated. The resulting solid was slurried in hexanes and filtered to afford 3-[4-

chloro-2-(toluene-4-sulfonylamino)-phenyl]-acrylic acid ethyl ester (28.3g, 93% yield) mp = 124-127 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 1.35 (t, 3, J = 7.2), 2.40 (s, 3), 4.27 (q, 2, J = 7.2), 6.12 (dd, 1, J = 15.9, 0.9), 7.20-7.39 (m, 4), 7.39 (d, 1, J = 8.6), 7.48-7.53 (m, 2), 7.62 (d, 2, J = 8.3). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 15.50, 22.79, 62.24, 122.48, 5 127.98, 128.49, 129.34, 129.50, 131.05, 136.82, 137.00, 137.73, 138.93, 145.55, 167.59. IR 3214, 1694, 1631, 1318, 1167 cm<sup>-1</sup>. Analysis calculated for C<sub>18</sub>H<sub>18</sub>ClNO<sub>4</sub>S: C, 56.91; H, 4.78; N, 3.69. Found: C, 57.10; H, 5.08; N, 3.70.

**Example 294**

[6-Chloro-2-(4-chloro-benzoyl)-1H-indol-3-yl]-acetic acid

10 To a solution of 3-[4-chloro-2-(toluene-4-sulfonylamino)-phenyl]-acrylic acid ethyl ester (13.0g, 34.2 mmol) in *N,N*-dimethylacetamide (120 ml) was added potassium carbonate (9.45g, 68.4 mmol) and 2-bromo-4'-chloroacetophenone (8.78g, 37.6 mmol) and the reaction was stirred at room temperature for 15 minutes. 1N Sodium hydroxide (130 ml) was added and the reaction mixture was heated to 100 °C for 8 hours. The reaction mixture was cooled to room temperature and poured into a separatory funnel and washed with methyl *t*-butyl ether (2 X 200 ml). The aqueous layer was acidified to pH 1 with 6N hydrochloric acid and was extracted with ethyl acetate (150 ml). The solvent was removed under reduced pressure and to the resulting oil was added isopropyl alcohol (24 ml) and water (48 ml). A solid precipitated and the slurry was stirred 12 hours. The precipitate was filtered, washed with water, and dried to provide [6-chloro-2-(4-chloro-benzoyl)-1H-indol-3-yl]-acetic acid (9.73g, 82%). mp 181-183 °C. <sup>1</sup>H NMR (400 MHz, d6-DMSO) δ 3.79 (s, 1), 7.08 (dd, 1, J = 8.5, 1.9), 7.42 (d, 1, J = 1.9), 7.60 (d, 2, J = 8.5), 7.62-7.73 (m, 3), 11.74 (bs, 1), 12.22 (bs, 1). <sup>13</sup>C NMR (75 MHz, d6-DMSO) δ 31.74, 113.25, 118.00, 121.93, 123.96, 127.69, 130.10, 131.30, 132.02, 133.59, 138.02, 138.37, 138.58, 25 173.20, 188.29. IR 3314, 1710, 1700, 1618, 1522, 1323, 1227, 1093, 941 cm<sup>-1</sup>. Analysis calculated for C<sub>17</sub>H<sub>11</sub>Cl<sub>2</sub>NO<sub>3</sub>: C, 58.64; H, 3.18; N, 4.02. Found: C, 58.58; H, 3.22; N, 3.93.

**Example 295**

30 3-{4-Chloro-2-[[2-(4-chloro-phenyl)-2-oxo-ethyl]-toluene-4-sulfonyl]-amino}-phenyl}-acrylic acid ethyl ester

To a solution of 3-[4-chloro-2-(toluene-4-sulfonylamino)-phenyl]-acrylic acid ethyl ester (3.00g, 7.90 mmol) in *N,N*-dimethylacetamide (15.0 ml) was added potassium carbonate (2.18g, 15.8 mmol) and 2-bromo-4'-chloroacetophenone (2.03g, 8.69 mmol). The reaction was stirred for 30 minutes, poured into 1N hydrochloric acid (30 ml) and extracted with methyl *t*-butyl ether (2 X 30 ml). The organic extracts were dried over magnesium sulfate, filtered, concentrated to a low volume. Hexanes was added and a solid precipitated. The precipitate was filtered to provide 3-{4-chloro-2-[[2-(4-chloro-phenyl)-2-oxo-ethyl]-toluene-4-sulfonyl]-amino}-phenyl}-acrylic acid ethyl ester (3.19g, 76%). mp = 162-165 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 1.38 (t, 3, J = 7.2), 2.47 (s, 3), 4.28 (q, 2, J = 7.2), 5.00 (bs, 2), 6.23 (d, 1, J = 16.0), 7.29-7.36 (m, 4), 7.47 (d, 2, J = 8.7), 7.54 (d, 1, J = 8.4), 7.59 (d, 2, J = 8.3), 7.74 (d, 1, J = 16.0), 7.88 (d, 2, J = 8.7). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 14.33, 21.62, 57.72, 60.66, 112.49, 120.69, 128.07, 129.21, 129.58, 129.70, 131.22, 132.80, 133.83, 134.80, 135.84, 138.55, 139.28, 140.38, 144.46, 166.02, 191.70. IR 1720, 1698, 1590, 1338, 1313, 1179, 1161, 1089 cm<sup>-1</sup>. Analysis calculated for C<sub>26</sub>H<sub>23</sub>Cl<sub>2</sub>NO<sub>5</sub>S: C, 58.65; H, 4.35; N, 2.63. Found: C, 58.74; H, 4.56; N, 2.72.

**Example 296**

**cis- and trans-[6-Chloro-2-(4-chloro-benzoyl)-1-(toluene-4-sulfonyl)-2,3-dihydro-1H-indol-3-yl]-acetic acid ethyl ester**

To 3-{4-chloro-2-[[2-(4-chloro-phenyl)-2-oxo-ethyl]-toluene-4-sulfonyl]-amino}-phenyl}-acrylic acid ethyl ester (1.00g, 1.88 mmol) in *N,N*-dimethylacetamide (5.0 ml) was added potassium carbonate (0.520g, 3.76 mmol). The reaction mixture was stirred for four hours, poured in 1N hydrochloric acid (30 ml) and extracted with methyl *t*-butyl ether (2 X 30 ml). The organic extracts were dried with magnesium sulfate, filtered, and concentrated. The resulting solid was purified by chromatography on silica gel (ethyl acetate/hexanes 20/80) to provide [6-chloro-2-(4-chloro-benzoyl)-1-(toluene-4-sulfonyl)-2,3-dihydro-1H-indol-3-yl]-acetic acid ethyl ester as a 1 to 9 mixture of *cis* and *trans* isomers (0.488g, 49%). Some of the <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) significant signals are: δ 1.09 (t, J = 7.2), 1.19 (t, J = 7.2), 2.44 (s), 5.40 (d, J = 4.0), 5.99 (d, J = 9.7), 6.92 (dd, J = 8.1, 1.1), 7.04 (dd, J = 8.1, 1.9), 7.52 (d, J = 8.4), 7.57 (d, J = 1.9), 7.73 (d, J = 8.3), 7.99 (d, J = 8.6). Lc-MS

analysis was performed on the mixture of diastereoisomers and indicated to products with identical mass of 531 ( $M+H^+$ ).

**Example 297**

**[6-Chloro-2-(4-chloro-benzoyl)-1H-indol-3-yl]-acetic acid ethyl ester**

5 To a solution of 3-[4-chloro-2-(toluene-4-sulfonylamino)-phenyl]-acrylic acid ethyl ester (3.00g, 7.90 mmol) in *N,N*-dimethylacetamide (15.0 ml) was added potassium carbonate (2.18g, 15.8 mmol) and 2-bromo-4'-chloroacetophenone (2.03g, 8.69 mmol). The reaction was stirred 30 minutes and 1,8-diazabicyclo[5.4.0]undec-7-ene (3.54 ml, 23.7 mmol) was added. The reaction mixture was stirred one hour.

10 poured into 1N hydrochloric acid (30 ml) and extracted with methyl *t*-butyl ether (2 X 30 ml). The organic extracts were dried with magnesium sulfate, filtered, and concentrated to provide a solid which was slurried in a mixture of methyl *t*-butyl ether and hexanes to afford [6-chloro-2-(4-chloro-benzoyl)-1H-indol-3-yl]-acetic acid ethyl ester (2.42g, 81%). mp = 186-188 °C.  $^1H$  NMR (300 MHz,  $CDCl_3$ )  $\delta$  1.27 (t, 2, J = 7.1), 3.80 (s, 2), 4.11 (q, 2, J = 7.1), 7.15 (ddd, 1, J = 8.5, 1.7, 0.5), 7.28-7.36 (m, 1), 7.48 (d, J = 8.3), 7.54-7.57 (m, 1), 7.77 (d, 2, J = 8.3), 9.16 (bs, 1).  $^{13}C$  NMR (75 MHz,  $CDCl_3$ )  $\delta$  15.42, 32.29, 62.45, 113.27, 117.60, 122.99, 123.23, 127.85, 130.12, 131.22, 133.61, 137.86, 138.13, 140.10, 172.45, 188.25. IR 3305, 1732, 1618, 1323 cm<sup>-1</sup>. Analysis calculated for  $C_{19}H_{15}Cl_2NO_3$ : C, 60.65; H, 4.02; N, 3.72. Found: C, 60.70, H, 3.97; N, 3.71.

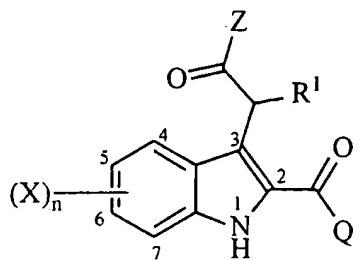
**Example 298**

**[6-Chloro-2-(4-chloro-benzoyl)-1H-indol-3-yl]-acetic acid**

To a solution of [6-chloro-2-(4-chloro-benzoyl)-1H-indol-3-yl]-acetic acid ethyl ester (200 mg, 0.532 mmol) in methanol (2 ml) and water (0.8 ml) was added 25 sodium hydroxide (137 mg, 3.43 mmol). The reaction mixture was stirred 24 hours, and was concentrated to a low volume. Water (4 ml) was added, the material was transferred to a separatory funnel and was washed with dichloromethane (5 ml). The aqueous layer was acidified to pH 1 with 1N hydrochloric acid and was extracted with ethyl acetate (15 ml). The organic layer was dried over magnesium sulfate, filtered, 30 and concentrate to afford [6-chloro-2-(4-chloro-benzoyl)-1H-indol-3-yl]-acetic acid (150 mg, 81%). The  $^1H$  NMR spectrum was identical with the one obtained for the

compound prepared by the method described in example 2.

The chemical structures of the compounds prepared in the Examples 1 to 292 are summarized in the following tables.

**TABLE**

5

Ex.#	(X) <sub>n</sub>	R <sup>1</sup>	Z	Q
1	6-Cl	H	ethoxy	phenyl
10	2	H	OH	phenyl
	3	H	ONa	phenyl
	4	H	OH	2-methylphenyl
	5	H	OH	3-methylphenyl
	6	H	OH	4-methylphenyl
	7	H	OH	3-chlorophenyl
15	8	H	methoxy	4-chlorophenyl
	9	H	OH	4-chlorophenyl
	10	H	OH	3-fluorophenyl
	11	H	OH	4-fluorophenyl
	12	H	OH	3-bromophenyl
	13	H	OH	4-bromophenyl
20	14	H	OH	3-CF <sub>3</sub> -phenyl
	15	H	OH	4-CF <sub>3</sub> -phenyl
	16	H	OH	3,4-dichlorophenyl
	17	4-Cl	OH	phenyl
	18	5-Cl	OH	3-methylphenyl
	19	5-Cl	OH	4-chlorophenyl
25	20	5-Cl	OH	3-chlorophenyl
	21	5-F	OH	4-chlorophenyl
	22	5-F	OH	3-chlorophenyl
	23	5-methoxy	OH	3-methylphenyl
	24	7-Cl	OH	phenyl
	25	4,5-di-Cl	OH	phenyl
30	26	4,6-di-Cl	OH	phenyl
	27	5,6-di-Cl	OH	phenyl

	Ex.#	(X) <sub>n</sub>	R <sup>1</sup>	Z	Q
5	28	6-Cl (racemic)	methyl	OH	phenyl
	29	6-Cl (less polar antipode)	methyl	OH	phenyl
	30	6-Cl (more polar antipode)	methyl	OH	phenyl
10	31	6-Cl	H	OH	4-methyl-2-pyridyl
	32	6-Cl	H	OH	5-methyl-2-pyridyl
	33	6-Cl	H	methoxy	4-chloro-2-pyridyl
	34	6-Cl	H	OH	4-chloro-2-pyridyl
	35	6-Cl	H	OH	2-pyridyl
15	36	5-Cl	H	OH	4-methyl-2-pyridyl
	37	5-Cl	H	methoxy	6-methyl-2-pyridyl
	38	5-Cl	H	OH	6-methyl-2-pyridyl
	39	6-Cl	H	OH	1-methyl-2-imidazolyl
	40	5-Cl	H	methoxy	2-thiazolyl
20	41	5-Cl	H	OH	2-thiazolyl
	42	6-Cl	H	methoxy	phenyl
	43	6-Cl	H	dimethylamino	phenyl
	44	6-Cl	H	methylamino	phenyl
	45	6-Cl	H	amino	phenyl
25	46	6-Cl	H	N-methoxy-N-methylamino	phenyl
	47	6-Cl	H	piperidino	phenyl
	48	6-Cl	H	4-methyl-1-piperazinyl	phenyl
	49	6-Cl	H	2-cyanoethylamino	phenyl
	50	6-Cl	H	2-HO-ethylamino	phenyl
30	51	6-Cl	H	morpholino	phenyl
	52	H	H	OH	4-chlorophenyl
	53	6-Cl	H	OH	2-furyl
	54	6-Cl	H	OH	cyclohexyl
	55	6-Cl	H	OH	4-methoxyphenyl
35	56	6-Cl	H	methoxy	4-methoxyphenyl
	57	6-Cl	H	methoxy	4-ethyl-2-pyridyl
	58	6-Cl	H	OH	4-ethyl-2-pyridyl
	59	5-Cl	H	methoxy	4-ethyl-2-pyridyl
	60	5-Cl	H	OH	4-ethyl-2-pyridyl
40	61	6-Cl	H	methoxy	4-isopropyl-2-pyridyl
	62	6-Cl	H	OH	4-isopropyl-2-pyridyl
	63	5-Cl	H	methoxy	4-isopropyl-2-pyridyl
	64	5-Cl	H	OH	4-isopropyl-2-pyridyl
	65	6-Cl	H	methoxy	4-n-propyl-2-pyridyl

Ex.#	(X) <sub>n</sub>	R <sup>1</sup>	Z	Q
5	66 6-Cl	H	OH	4-n-propyl-2-pyridyl
	67 5-Cl	H	methoxy	4-n-propyl-2-pyridyl
	68 5-Cl	H	OH	4-n-propyl-2-pyridyl
	69 6-Cl	H	methoxy	4-tert-butyl-2-pyridyl
	70 6-Cl	H	OH	4-tert-butyl-2-pyridyl
10	71 5-Cl	H	methoxy	4-tert-butyl-2-pyridyl
	72 5-Cl	H	OH	4-tert-butyl-2-pyridyl
	73 6-Cl	H	methoxy	3-methyl-2-pyridyl
	74 6-Cl	H	OH	3-methyl-2-pyridyl
	75 5-Cl	H	methoxy	3-methyl-2-pyridyl
15	76 5-Cl	H	OH	3-methyl-2-pyridyl
	77 6-Cl	H	methoxy	6-methyl-2-pyridyl
	78 6-Cl	H	OH	6-methyl-2-pyridyl
	79 5-Cl	H	methoxy	5-methyl-2-pyridyl
	80 5-Cl	H	OH	5-methyl-2-pyridyl
20	81 6-Cl	H	methoxy	5-CF <sub>3</sub> -2-pyridyl
	82 6-Cl	H	OH	5-CF <sub>3</sub> -2-pyridyl
	83 5-Cl	H	methoxy	5-CF <sub>3</sub> -2-pyridyl
	84 5-Cl	H	OH	5-CF <sub>3</sub> -2-pyridyl
	85 5-Cl	H	methoxy	5-Cl-2-pyridyl
25	86 5-Cl	H	OH	5-Cl-2-pyridyl
	87 6-Cl	H	methoxy	5-Cl-2-pyridyl
	88 6-Cl	H	OH	5-Cl-2-pyridyl
	89 5-Cl	H	methoxy	4-Cl-2-pyridyl
	90 5-Cl	H	OH	4-Cl-2-pyridyl
30	91 6-Cl	H	methoxy	3-pyridyl
	92 6-Cl	H	OH	3-pyridyl
	93 6-Cl	H	methoxy	4-pyridyl
	94 6-Cl	H	OH	4-pyridyl
	95 6-Cl	H	methoxy	4-hydroxymethyl-2-pyridyl
35	96 6-Cl	H	OH	4-hydroxymethyl-2-pyridyl
	97 5-Cl	H	methoxy	4-hydroxymethyl-2-pyridyl
	98 5-Cl	H	OH	4-hydroxymethyl-2-pyridyl
	99 5-Cl	H	methoxy	3,4-dimethyl-2-pyridyl
	100 5-Cl	H	OH	3,4-dimethyl-2-pyridyl
40	101 5-Cl	H	methoxy	4,5-dimethyl-2-pyridyl
	102 5-Cl	H	OH	4,5-dimethyl-2-pyridyl
	103 6-Cl	H	methoxy	4,5-dimethyl-2-pyridyl
	104 6-Cl	H	OH	4,5-dimethyl-2-pyridyl
	105 6-Cl	H	methoxy	4-methoxy-2-pyridyl
45	106 6-Cl	H	OH	4-methoxy-2-pyridyl

Ex.#	(X) <sub>n</sub>	R <sup>1</sup>	Z	Q
5	107 5-Cl	H	methoxy	4-methoxy-2-pyridyl
	108 5-Cl	H	OH	4-methoxy-2-pyridyl
	109 6-Cl	H	methoxy	3,5-dimethyl-2-pyridyl
	110 6-Cl	H	OH	3,5-dimethyl-2-pyridyl
	111 5-Cl	H	methoxy	3-F-4-ethyl-2-pyridyl
	112 5-Cl	H	OH	3-F-4-ethyl-2-pyridyl
10	113 6-Cl	H	methoxy	3-F-4-ethyl-2-pyridyl
	114 6-Cl	H	OH	3-C <sub>2</sub> H <sub>5</sub> O-4-ethyl-2-pyridyl
	115 6-Cl	H	methoxy	3-Cl-4-ethyl-2-pyridyl
	116 6-Cl	H	OH	3-Cl-4-ethyl-2-pyridyl
	117 5-Cl	H	methoxy	3-Cl-4-ethyl-2-pyridyl
	118 5-Cl	H	OH	3-Cl-4-ethyl-2-pyridyl
15	119 5-Cl	H	methoxy	4,6-dimethyl-2-pyridyl
	120 5-Cl	H	OH	4,6-dimethyl-2-pyridyl
	121 6-Cl	H	methoxy	4,6-dimethyl-2-pyridyl
	122 6-Cl	H	OH	4,6-dimethyl-2-pyridyl
	123 5,6-di-Cl	H	methoxy	4-methyl-2-pyridyl
	124 5,6-di-Cl	H	OH	4-methyl-2-pyridyl
20	125 5-methyl	H	methoxy	4-methyl-2-pyridyl
	126 5-methyl	H	OH	4-methyl-2-pyridyl
	127 5-F	H	methoxy	4-methyl-2-pyridyl
	128 5-F	H	OH	4-methyl-2-pyridyl
	129 5-methoxy	H	methoxy	4-methyl-2-pyridyl
	130 5-methoxy	H	OH	4-methyl-2-pyridyl
25	131 6-methoxy	H	methoxy	4-methyl-2-pyridyl
	132 6-methoxy	H	OH	4-methyl-2-pyridyl
	133 5-ethyl	H	methoxy	4-methyl-2-pyridyl
	134 5-ethyl	H	OH	4-methyl-2-pyridyl
	135 5-ethyl	H	methoxy	4-ethyl-2-pyridyl
	136 5-ethyl	H	OH	4-ethyl-2-pyridyl
30	137 6-ethyl	H	methoxy	4-methyl-2-pyridyl
	138 6-ethyl	H	OH	4-methyl-2-pyridyl
	139 5-isopropyl	H	methoxy	4-ethyl-2-pyridyl
	140 5-isopropyl	H	OH	4-methyl-2-pyridyl
	141 6-CF <sub>3</sub>	H	methoxy	4-methyl-2-pyridyl
	142 6-CF <sub>3</sub>	H	OH	4-methyl-2-pyridyl
35	143 5-tert-butyl	H	methoxy	4-methyl-2-pyridyl
	144 5-tert-butyl	H	OH	4-methyl-2-pyridyl
	145 5-CF <sub>3</sub> O	H	methoxy	4-methyl-2-pyridyl
	146 5-CF <sub>3</sub> O	H	OH	4-methyl-2-pyridyl
	147 5-CF <sub>3</sub> O	H	methoxy	4-ethyl-2-pyridyl
	148 5-CF <sub>3</sub> O	H	OH	4-ethyl-2-pyridyl

Ex.#	(X) <sub>n</sub>	R <sup>1</sup>	Z	Q
5	149 6-methyl	H	methoxy	4-methyl-2-pyridyl
	150 6-methyl	H	OH	4-methyl-2-pyridyl
	151 5-CF <sub>3</sub>	H	methoxy	4-methyl-2-pyridyl
	152 5-CF <sub>3</sub>	H	OH	4-methyl-2-pyridyl
	153 5-CF <sub>3</sub>	H	methoxy	4-ethyl-2-pyridyl
	154 5-CF <sub>3</sub>	H	OH	4-ethyl-2-pyridyl
10	155 H	H	methoxy	phenyl
	156 H	H	OH	phenyl
	157 6-methyl	H	methoxy	4-chlorophenyl
	158 6-methyl	H	OH	4-chlorophenyl
	159 5-methyl	H	OH	4-chlorophenyl
	160 6-methoxy	H	methoxy	4-chlorophenyl
15	161 6-methoxy	H	OH	4-chlorophenyl
	162 6-CF <sub>3</sub>	H	OH	4-chlorophenyl
	163 5-ethyl	H	methoxy	4-chlorophenyl
	164 5-ethyl	H	OH	4-chlorophenyl
	165 5-methoxy	H	methoxy	4-chlorophenyl
	166 5-methoxy	H	OH	4-chlorophenyl
20	167 5-isopropyl	H	methoxy	4-chlorophenyl
	168 5-isopropyl	H	OH	4-chlorophenyl
	169 5-CF <sub>3</sub>	H	methoxy	4-chlorophenyl
	170 5-CF <sub>3</sub>	H	OH	4-chlorophenyl
	171 5-CF <sub>3</sub> O	H	methoxy	4-chlorophenyl
	172 5-CF <sub>3</sub> O	H	OH	4-chlorophenyl
25	173 6-Cl	H	methoxy	2-methoxyphenyl
	174 6-Cl	H	OH	2-methoxyphenyl
	175 6-Cl	H	methoxy	3-methoxyphenyl
	176 6-Cl	H	OH	3-methoxyphenyl
	177 6-Cl	H	methoxy	3-benzyloxyphenyl
	178 6-Cl	H	OH	3-benzyloxyphenyl
30	179 6-Cl	H	methoxy	3-hydroxyphenyl
	180 6-Cl	H	OH	3-hydroxyphenyl
	181 6-Cl	H	methoxy	4-benzyloxyphenyl
	182 6-Cl	H	OH	4-benzyloxyphenyl
	183 6-Cl	H	methoxy	4-hydroxyphenyl
	184 6-Cl	H	OH	4-hydroxyphenyl
35	185 6-Cl	H	methoxy	4-isopropoxyphenyl
	186 6-Cl	H	OH	4-isopropoxyphenyl
	187 6-Cl	H	methoxy	4-biphenyl
	188 6-Cl	H	OH	4-biphenyl
	189 6-Cl	H	methoxy	4-CF <sub>3</sub> O-phenyl
	190 6-Cl	H	OH	4-CF <sub>3</sub> O-phenyl

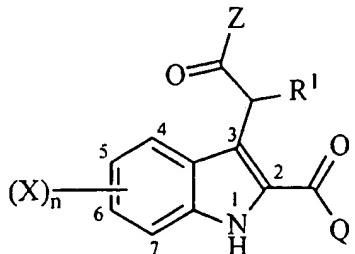
Ex.#	(X) <sub>n</sub>	R <sup>1</sup>	Z	Q
5	191 5-Cl	H	methoxy	4-CF <sub>3</sub> O-phenyl
	192 5-Cl	H	OH	4-CF <sub>3</sub> O-phenyl
	193 5-Cl	H	methoxy	4-methoxyphenyl
	194 5-Cl	H	OH	4-methoxyphenyl
	195 6-Cl	H	methoxy	4-nitrophenyl
	196 6-Cl	H	OH	4-nitrophenyl
10	197 6-Cl	H	methoxy	4-methyl-S(O) <sub>2</sub> -phenyl
	198 6-Cl	H	OH	4-methyl-S(O) <sub>2</sub> -phenyl
	199 6-Cl	H	methoxy	4-methyl-S(O) <sub>2</sub> -NH-phenyl
	200 6-Cl	H	OH	4-methyl-S(O) <sub>2</sub> -NH-phenyl
	201 6-Cl	H	OH	2-chlorophenyl
	202 6-Cl	H	OH	2,4-dichlorophenyl
15	203 6-Cl	H	methoxy	3-F-4-Cl-phenyl
	204 6-Cl	H	OH	3-F-4-Cl-phenyl
	205 6-Cl	H	methoxy	4-cyanophenyl
	206 6-Cl	H	methoxy	4-bromophenyl
	207 6-Cl	H	methoxy	4-(2-thienyl)phenyl
	208 6-Cl	H	OH	4-(2-thienyl)phenyl
20	209 6-Cl	H	methoxy	4-(2-furyl)phenyl
	210 6-Cl	H	OH	4-(2-furyl)phenyl
	211 6-Cl	H	methoxy	4-(3-pyridyl)phenyl
	212 6-Cl	H	OH	4-(3-pyridyl)phenyl
	213 6-Cl	H	methoxy	4-(2-thiazolyl)phenyl
	214 6-Cl	H	OH	4-(2-thiazolyl)phenyl
25	215 6-Cl	H	methoxy	3-bromophenyl
	216 6-Cl	H	methoxy	3-(2-furyl)phenyl
	217 6-Cl	H	OH	3-(2-furyl)phenyl
	218 6-Cl	methyl	methoxy	4-chlorophenyl
	219 6-Cl	methyl	OH	4-chlorophenyl
	220 5-Cl	H	methoxy	isoquinolin-3-yl
30	221 5-Cl	H	OH	isoquinolin-3-yl
	222 6-Cl	H	methoxy	isoquinolin-3-yl
	223 6-Cl	H	OH	isoquinolin-3-yl
	224 5-Cl	H	methoxy	5-methyl-3-isoxazolyl
	225 5-Cl	H	OH	5-methyl-3-isoxazolyl
	226 6-Cl	H	methoxy	5-methyl-3-isoxazolyl
35	227 6-Cl	H	OH	5-methyl-3-isoxazolyl
	228 5-Cl	H	methoxy	4-methyl-5-(1,2,3-thiadiazolyl)
	229 5-Cl	H	OH	4-methyl-5-(1,2,3-thiadiazolyl)
	230 6-Cl	H	methoxy	4-methyl-5-(1,2,3-thiadiazolyl)
	231 6-Cl	H	OH	4-methyl-5-(1,2,3-thiadiazolyl)
	232 5-Cl	H	methoxy	5-methyl-2-thiazolyl

Ex.#	(X) <sub>n</sub>	R <sup>1</sup>	Z	Q
5	233 5-Cl	H	OH	5-methyl-2-thiazolyl
	234 6-Cl	H	methoxy	5-methyl-2-thiazolyl
	235 6-Cl	H	OH	5-methyl-2-thiazolyl
	236 6-Cl	H	OH	2-thienyl
	237 6-Cl	H	methoxy	3-(HO)(CH <sub>3</sub> ) <sub>2</sub> C-2-furyl
	238 6-Cl	H	OH	3-(HO)(CH <sub>3</sub> ) <sub>2</sub> C-2-furyl
10	239 6-Cl	H	methoxy	3-methoxymethyl-2-furyl
	240 6-Cl	H	OH	3-methoxymethyl-2-furyl
	241 6-Cl	H	OH	1-methyl-2-imidazolyl
	242 6-Cl	H	methoxy	1-methyl-2-imidazolyl
	243 5-Cl	H	methoxy	1-methyl-2-imidazolyl
	244 5-Cl	H	OH	1-methyl-2-imidazolyl
15	245 5-Cl	H	methoxy	2-imidazolyl
	246 5-Cl	H	OH	2-imidazolyl
	247 6-Cl	H	methoxy	2-imidazolyl
	248 6-Cl	H	OH	2-imidazolyl
	249 5-Cl	H	methoxy	4-methyl-2-thiazolyl
	250 5-Cl	H	OH	4-methyl-2-thiazolyl
20	251 5-Cl	H	methoxy	1-methyl-2-pyrrolyl
	252 5-Cl	H	OH	1-methyl-2-pyrrolyl
	253 5-Cl	H	methoxy	2-methyl-4-thiazolyl
	254 5-Cl	H	OH	2-methyl-4-thiazolyl
	255 5-Cl	H	methoxy	5-thiazolyl
	256 5-Cl	H	OH	5-thiazolyl
25	257 6-Cl	H	methoxy	4-methyl-2-thiazolyl
	258 6-Cl	H	OH	4-methyl-2-thiazolyl
	259 5-Cl	H	methoxy	3-carboxyl-5-isoxazolyl
	260 5-Cl	H	OH	3-carboxyl-5-isoxazolyl
	261 6-Cl	H	methoxy	cyclopropyl
	262 6-Cl	H	OH	cyclopropyl
30	263 6-Cl	H	methoxy	cyclobutyl
	264 6-Cl	H	OH	cyclobutyl
	265 5-tert-butyl	H	methoxy	4-chlorophenyl
	266 5-tert-butyl	H	OH	4-chlorophenyl
	267 6-Cl	H	dimethylamino	4-methyl-2-pyridyl
	268 6-Cl	H	methylamino	4-methyl-2-pyridyl
35	269 5-Cl	H	HO-(CH <sub>2</sub> ) <sub>2</sub> -NH-	4-methyl-2-pyridyl
	270 5-Cl	H	methoxyamino	4-methyl-2-pyridyl
	271 5-Cl	H	1-piperazinyl	4-methyl-2-pyridyl
	272 5-Cl	H	H <sub>2</sub> N-(CH <sub>2</sub> ) <sub>2</sub> -NH-	4-methyl-2-pyridyl
	273 5-Cl	H	3-amino-1-pyrrolidinyl	4-methyl-2-pyridyl

	Ex.#	(X) <sub>n</sub>	R <sup>1</sup>	Z	Q
5	274	5-F,6-Cl	H	methoxy	4-chlorophenyl
	275	5-F,6-Cl	H	OH	4-chlorophenyl
	276	5-F,6-Cl	H	methoxy	4-methyl-2-pyridyl
	277	5-F,6-Cl	H	OH	4-methyl-2-pyridyl
10	278	6-Cl	H	methoxy	4-(HO)(H <sub>3</sub> C)CH-2-pyridyl
	279	6-Cl	H	OH	4-(HO)(H <sub>3</sub> C)CH-2-pyridyl
	280	6-Cl	H	OH	4-ethyl-3-F-2-pyridyl
	281	6-Cl	H	OH	2-nitrophenyl
15	282	6-Cl	H	OH	2,4-dimethoxyphenyl
	283	6-Cl	H	OH	4-CHF <sub>2</sub> O-phenyl
	284	6-Cl	H	OH	2,5-dimethoxyphenyl
	285	5-acetyl	H	methoxy	4-Cl-phenyl
20	286	5-acetyl	H	OH	4-Cl-phenyl
	287	6-F	H	methoxy	4-methyl-2-pyridyl
	288	6-F	H	OH	4-methyl-2-pyridyl
	289	6-F	H	methoxy	4-Cl-phenyl
20	290	6-F	H	OH	4-Cl-phenyl
	291	5-CH <sub>3</sub> S-	H	methoxy	4-methyl-2-pyridyl
	292	5-CH <sub>3</sub> S-	H	OH	4-methyl-2-pyridyl

CLAIMS

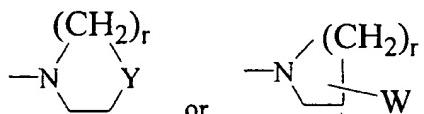
1. A compound of the following formula:



(I)

5 or the pharmaceutically acceptable salts thereof wherein

Z is OH, C<sub>1-6</sub> alkoxy, -NR<sup>2</sup>R<sup>3</sup> or a group of the formula (II) or (III):



(II)

(III)

wherein r is 1, 2, 3 or 4, Y is a direct bond, O, S or NR<sup>4</sup>, and W is OH or -NR<sup>2</sup>R<sup>3</sup>.

10 Q is selected from the following:

(a) phenyl optionally substituted with one, two or three substituents independently selected from

(a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>R<sup>3</sup>, acetyl-COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>1-4</sub> cycloalkyl,

(a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

(a-3) 5-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub>

<sup>4</sup> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

(a-4) 6-membered monocyclic aromatic group optionally substituted with

5 one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

10 (b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),

15 (c) a 5-membered monocyclic aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);

20 (d) C<sub>3-7</sub> cycloalkyl optionally substituted with one or two substituents independently selected from OH, C<sub>1-4</sub> alkyl, halo and halo-substituted C<sub>1-4</sub> alkyl; and

(e) a benzo-fuzed heterocycle optionally substituted with one, two or three substituents independently selected from the group (a-1);

R<sup>1</sup> is hydrogen, C<sub>1-4</sub> alkyl or halo;

25 R<sup>2</sup> and R<sup>3</sup> are independently H, OH, C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkyl substituted with halo, OH, C<sub>1-4</sub> alkoxy, NH<sub>2</sub> or CN;

R<sup>4</sup> is hydrogen or C<sub>1-4</sub> alkyl;

X is independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino,

30 C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>NR<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub>

alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl; and

n is 0, 1, 2, 3 or 4.

2. A compound according to claim 1, wherein

Z is OH, C<sub>1-6</sub> alkoxy, dimethylamino, methylamino, amino, N-methoxy-N-methylamino, 2-cyanoethylamino, 2-hydroxyethylamino, pyrrolidinyl, piperidino, piperazinyl, N-methyl-piperazinyl, morpholino, methoxyamino, piperazinyl, aminopyrrolidinyl or aminoethylamino.

3. A compound according to claim 2, wherein

Z is OH or C<sub>1-6</sub> alkoxy; and

10 Q is selected from the following:

(a) phenyl optionally substituted with one, two or three substituents independently selected from

(a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>1</sup>R<sup>2</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>1-4</sub> cycloalkyl,

(a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

(a-3) 5-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

(a-4) 6-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-

substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

- 5 (b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),

10 (c) a 5-membered monocyclic aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);

15 (d) C<sub>3-7</sub> cycloalkyl selected from cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl, and the said cycloalkyl being optionally substituted with one substituent selected from OH, methyl, ethyl, propyl, F, Cl and CF<sub>3</sub>; and

20 (e) a benzo-fused heterocycle selected from quinolyl, isoquinolyl, cinnolinyl, quinoxaliny, benzoimidazolyl, benzothiazolyl, benzoxazolyl, benzofuranyl, benzothiophenyl and indolyl, and the benzo-fused heterocycle being optionally substituted with one, two, or three substituents independently selected from the group (a-1).

4. A compound according to claim 3, wherein

**Q** is selected from the following:

- (a) phenyl optionally substituted with one, two or three substituents independently selected from

25 (a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>R<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl,

30 (a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally

substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

- 5                   (a-3) 5-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
- 10                  (a-4) 6-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
- 15                  (b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),
- 20                  (c) a 5-membered monocyclic aromatic group containing one heteroatom, selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);
- 25                  (d) cyclopropyl, cyclobutyl and cyclohexyl; and
- (e) quinolyl or isoquinolyl, and said quinolyl or isoquinolyl being optionally substituted with one substituent selected from the group halo, C<sub>1-4</sub> alkyl, NH<sub>2</sub>, OH, C<sub>1-4</sub> alkoxy and C<sub>1-4</sub> halo-substituted alkyl.

5. A compound according to claim 4, wherein

30 Z is OH, C<sub>1-6</sub> alkoxy;

Q is selected from the following:

- (a) phenyl optionally substituted with one, two or three substituents independently selected from
- (a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>R<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl,
- (a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl; halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
- (a-3) 5-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
- (a-4) 6-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
- (b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),
- (c) a 5-membered monocyclic aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three

substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4); and

(e) isoquinolyl;

$R^1$  is hydrogen or  $C_{1-4}$  alkyl;

5     $R^2$  and  $R^3$  are independently H or methyl;

**X** is independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>NR<sup>3</sup>, acetyl, -COOR<sup>4</sup>, C<sub>1-4</sub> alkylsulfonylamino and C<sub>1-4</sub>

10 cycloalkyl; and

**n** is 0, 1, 2, or 3.

6. A compound according to claim 5, wherein

Z is OH, methoxy, ethoxy, n-propoxy, iso-propoxy, n-butoxy, iso-butoxy or tert-butoxy;

15 Q is selected from the following:

(a) phenyl optionally substituted with one or two substituents independently selected from

(a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, HO-(C<sub>1-4</sub>) alkyl, alkoxy-C<sub>1-4</sub> alkyl, -COOH, C<sub>1-4</sub> alkylsulfonylamino, nitro, alkylsulfonyl and cyano,

alkoxy-C<sub>1-4</sub> alkyl, -COOH, C<sub>1-4</sub> alkylsulfonylamino, nitro, -NO<sub>2</sub>,  
alkylsulfonyl and cyano,

25 substituted C<sub>1-4</sub> alkoxy and NH<sub>2</sub>,

30 substituent selected from C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl,  
halo, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy and NH<sub>2</sub>.

- (a-4) 6-membered monocyclic aromatic group selected from pyridyl, pyrazinyl, pyrimidinyl and pyridazinyl, and the 6-membered monocyclic aromatic group optionally being substituted with one substituent selected from C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, halo, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy and NH<sub>2</sub>,
- 5 (b) a 6-membered monocyclic aromatic group selected from pyridyl, pyrazinyl, pyrimidinyl and pyridazinyl, and said monocyclic aromatic group being optionally substituted with one or two substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),
- 10 (c) a 5-membered monocyclic aromatic group selected from imidazolyl, thiazolyl, furyl, thienyl, pyrrolyl, tetrazolyl, triazolyl, oxazolyl, isoxazolyl, thiadiazolyl and pyrazolyl, and said monocyclic aromatic group being optionally substituted with one or two substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);
- 15 R<sup>1</sup> is hydrogen, methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl or tert-butyl; X is independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl and aminosulfonyl; and
- 20 n is 0, 1, 2, or 3.
7. A compound according to claim 6, wherein
- Z is OH, methoxy, ethoxy, n-propoxy, iso-propoxy, n-butoxy, iso-butoxy or tert-butoxy;
- Q is selected from the following:
- 25 (a) phenyl optionally substituted with one or two substituents independently selected from
- (a-1) fluoro, chloro, bromo, iodo, methyl, ethyl, propyl, butyl, CH<sub>2</sub>F, CHF<sub>2</sub>, CF<sub>3</sub>, methoxy, ethoxy, n-propoxy, n-butoxy, isopropoxy, CH<sub>2</sub>F-O-, CHF<sub>2</sub>-O-, CF<sub>3</sub>-O-, methylthio, ethylthio, hydroxymethyl, methoxymethyl, methoxyethyl, ethoxymethyl, hydroxy, nitro, methylsulfonyl, cyano, (HO)(H<sub>3</sub>C)<sub>2</sub>C-, acetyl and
- 30

methylsulfonylamino,

(a-2) phenyl or benzyloxy, and the phenyl or phenyl moiety of benzyloxy being optionally substituted with one substituent selected from methyl, ethyl, propyl, CF<sub>3</sub>, F, Cl, OH, methoxy, ethoxy and NH<sub>2</sub>,

5 (a-3) 5-membered monocyclic aromatic group selected from furyl, thienyl and pyrrolyl, and the 5-membered monocyclic aromatic group optionally being substituted with one substituent selected from methyl, ethyl, propyl, CF<sub>3</sub>, F, Cl, OH, methoxy, ethoxy and NH<sub>2</sub>.

10 (a-4) pyridyl optionally substituted with one substituent selected from methyl, ethyl, propyl, CF<sub>3</sub>, F, Cl, OH, methoxy, ethoxy and NH<sub>2</sub>.

(b) pyridyl optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-1), (a-2), (a-3) and (a-4),

15 (c) imidazolyl, thiazolyl, furyl, thienyl, isoxazolyl, 1,2,3-thiadiazolyl or pyrrolyl, and said imidazolyl, thiazolyl, furyl, thienyl, isoxazolyl, 1,2,3-thiadiazolyl or pyrrolyl being optionally substituted with one or two substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);

R<sup>1</sup> is hydrogen, methyl, ethyl, n-propyl, iso-propyl;

20 X is independently selected from fluoro, chloro, bromo, methyl, ethyl, propyl, butyl, CH<sub>2</sub>F, CHF<sub>2</sub>, CF<sub>3</sub>, methoxy, CF<sub>3</sub>O or ethoxy; and  
n is 0, 1 or 2.

8. A compound according to claim 7, wherein

Z is OH, ethoxy or methoxy; Q is phenyl, chlorophenyl, fluorophenyl, bromophenyl, 25 methylphenyl, methoxyphenyl, (furyl)phenyl, trifluoromethylphenyl, trifluoromethoxyphenyl, pyridyl, methylpyridyl, ethylpyridyl, propylpyridyl, dimethylpyridyl, chloropyridyl, fluoropyridyl, trifluoromethylpyridyl, methoxypyridyl, (ethyl)(ethoxy)pyridyl, (chloro)(ethyl)pyridyl, thiazolyl, methylthiazolyl, furyl, methoxymethylfuryl, isoquinolyl, cyclohexyl, methoxyphenyl, (fluoro)(ethyl)pyridyl, 30 dimethylpyridyl or (ethoxy)(ethyl)pyridyl;

R<sup>1</sup> is hydrogen; X is fluoro, chloro, methyl, ethyl, isopropyl, tert-butyl, CF<sub>3</sub> or

methoxy; and **n** is 1 or 2.

9. A compound according to claim 8, wherein  
**Z** is OH, ethoxy or methoxy; **Q** is phenyl, chlorophenyl, pyridyl, methylpyridyl, ethylpyridyl, propylpyridyl or chloropyridyl; **R<sup>1</sup>** is hydrogen; **X** is fluoro, chloro, 5 methyl or CF<sub>3</sub>; and **n** is 1 or 2.
10. A compound according to claim 1 selected from  
ethyl (2-benzoyl-6-chloro-1H-indol-3-yl)acetate;  
(2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid;  
(2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid, sodium salt;  
10 [6-chloro-2-(2-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetate;  
15 [6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-fluorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-fluorobenzoyl)-1H-indol-3-yl]acetic acid;  
[2-(3-bromobenzoyl)-6-chloro-1H-indol-3-yl]acetic acid;  
[2-(4-bromobenzoyl)-6-chloro-1H-indol-3-yl]acetic acid;  
20 [6-chloro-2-(3-trifluoromethylbenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-trifluoromethylbenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3,4-dichlorobenzoyl)-1H-indol-3-yl]acetic acid;  
(2-benzoyl-4-chloro-1H-indol-3-yl)acetic acid;  
[5-chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
25 [5-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
[2-(3-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
[5-methoxy-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
30 (2-benzoyl-7-chloro-1H-indol-3-yl)acetic acid;  
(2-benzoyl-4,5-dichloro-1H-indol-3-yl)acetic acid;

- (2-benzoyl-4,6-dichloro-1H-indol-3-yl)acetic acid;  
(2-benzoyl-5,6-dichloro-1H-indol-3-yl)acetic acid;  
*dl*-2-(2-benzoyl-6-chloro-1H-indol-3-yl)propanoic acid;  
less polar antipode, 2-(2-benzoyl-6-chloro-1H-indol-3-yl)propanoic acid;  
5 more polar antipode, 2-(2-benzoyl-6-chloro-1H-indol-3-yl)propanoic acid:  
[6-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
10 [6-chloro-2-(pyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
15 methyl [5-chloro-2-(thiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(thiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl (2-benzoyl-6-chloro-1H-indol-3-yl)acetate;  
(2-benzoyl-6-chloro-1H-indol-3-yl)-*N,N*-dimethylacetamide;  
(2-benzoyl-6-chloro-1H-indol-3-yl)-*N*-methylacetamide;  
20 (2-benzoyl-6-chloro-1H-indol-3-yl)acetamide;  
(2-benzoyl-6-chloro-1H-indol-3-yl)-*N*-methoxy-*N*-methylacetamide;  
2-(2-benzoyl-6-chloro-1H-indol-3-yl)-1-piperidino-1-ethanone;  
2-(2-benzoyl-6-chloro-1H-indol-3-yl)-1-(4-methyl-1-piperazinyl)-1-ethanone;  
(2-benzoyl-6-chloro-1H-indol-3-yl)-*N*-(2-cyanoethyl)acetamide;  
25 (2-benzoyl-6-chloro-1H-indol-3-yl)-*N*-(2-hydroxyethyl)acetamide;  
2-(2-benzoyl-6-chloro-1H-indol-3-yl)-1-morpholino-1-ethanone;  
[2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(2-furylcarbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(cyclohexanecarbonyl)-1H-indol-3-yl]acetic acid;  
30 methyl [6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;

- methyl [6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 5 methyl [6-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 10 [6-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [2-(4-*tert*-butylpyridine-2-carbonyl)-6-chloro-1H-indol-3-yl]acetate;  
[2-(4-*tert*-butylpyridine-2-carbonyl)-6-chloro-1H-indol-3-yl]acetic acid;
- 15 methyl [2-(4-*tert*-butylpyridine-2-carbonyl)-5-chloro-1H-indol-3-yl]acetate;  
[2-(4-*tert*-butylpyridine-2-carbonyl)-5-chloro-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(3-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(3-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(3-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 20 [5-chloro-2-(3-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 25 methyl [6-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;  
[5-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 30 [5-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;

- [6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(pyridine-3-carbonyl)-1H-indol-3-yl]acetate;
- 5 [6-chloro-2-(pyridine-3-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(pyridine-4-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(pyridine-4-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[4-(hydroxymethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[4-(hydroxymethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;
- 10 methyl [5-chloro-2-[4-(hydroxymethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;  
[5-chloro-2-[4-(hydroxymethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(3,4-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(3,4-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 15 [5-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 20 methyl [5-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(3,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(3,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetate.
- 25 [5-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(3-ethoxy-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 30 methyl [5-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;

- methyl [5-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 5   methyl [5,6-dichloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5,6-dichloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 10   [5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 15   methyl [5-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-ethyl-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-ethyl-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 20   [6-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-isopropyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-isopropyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [2-(4-methylpyridine-2-carbonyl)-6-trifluoromethyl-1H-indol-3-yl]acetate;  
[2-(4-methylpyridine-2-carbonyl)-6-trifluoromethyl-1H-indol-3-yl]acetic acid;
- 25   methyl [5-*tert*-butyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-*tert*-butyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [2-(4-methylpyridine-2-carbonyl)-5-trifluoromethoxy-1H-indol-3-yl]acetate;  
[2-(4-methyl-2-pyridine-2-carbonyl)-5-trifluoromethoxy-1H-indol-3-yl]acetic acid;  
methyl [2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethoxy-1H-indol-3-yl]acetate;
- 30   [2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethoxy-1H-indol-3-yl]acetic acid;  
methyl [6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;

- [6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [2-(4-methylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetate;  
[2-(4-methylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
methyl [2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetate;
- 5 [2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
methyl (2-benzoyl-1H-indol-3-yl)acetate;  
(2-benzoyl-1H-indol-3-yl)acetic acid;  
methyl [2-(4-chlorobenzoyl)-6-methyl-1H-indol-3-yl]acetate;  
[2-(4-chlorobenzoyl)-6-methyl-1H-indol-3-yl]acetic acid;
- 10 [2-(4-chlorobenzoyl)-5-methyl-1H-indol-3-yl]acetic acid;  
methyl [6-methoxy-2-(4-chlorobenzoyl)-1H-indol-3-yl] acetate;  
[6-methoxy-2-(4-chlorobenzoyl)-1H-indol-3-yl] acetic acid;  
[2-(4-chlorobenzoyl)-6-trifluoromethyl-1H-indol-3-yl]acetic acid;  
methyl [2-(4-chlorobenzoyl)-5-ethyl-1H-indol-3-yl]acetate;
- 15 [2-(4-chlorobenzoyl)-5-ethyl-1H-indol-3-yl]acetic acid;  
methyl [2-(4-chlorobenzoyl)-5-methoxy-1H-indol-3-yl]acetate;  
[2-(4-chlorobenzoyl)-5-methoxy-1H-indol-3-yl]acetic acid;  
methyl [2-(4-chlorobenzoyl)-5-isopropyl-1H-indol-3-yl]acetate;  
[2-(4-chlorobenzoyl)-5-isopropyl-1H-indol-3-yl]acetic acid;
- 20 methyl [2-(4-chlorobenzoyl)-5-trifluoromethyl-1H-indol-3-yl]acetate;  
[2-(4-chlorobenzoyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
methyl [2-(4-chlorobenzoyl)-5-trifluoromethoxy-1H-indol-3-yl] acetate;  
[2-(4-chlorobenzoyl)-5-trifluoromethoxy-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(2-methoxybenzoyl)-1H-indol-3-yl]acetate;
- 25 [6-chloro-2-(2-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(3-methoxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(3-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(3-benzyloxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(3-benzyloxybenzoyl)-1H-indol-3-yl]acetic acid;
- 30 methyl [6-chloro-2-(3-hydroxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(3-hydroxybenzoyl)-1H-indol-3-yl]acetic acid;

- methyl [6-chloro-2-(4-benzyloxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-benzyloxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-hydroxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-hydroxybenzoyl)-1H-indol-3-yl]acetic acid;
- 5    methyl [6-chloro-2-(4-isopropoxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-isopropoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-phenylbenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-phenylbenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetate;
- 10   [6-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;
- 15   methyl [6-chloro-2-(4-nitrobenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-nitrobenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[(4-methylsulfonyl)benzoyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[(4-methylsulfonyl)benzoyl]-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[4-(methylsulfonylamino)benzoyl]-1H-indol-3-yl]acetate;
- 20   [6-chloro-2-[4-(methylsulfonylamino)benzoyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(2-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(2,4-dichlorobenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-chloro-3-fluorobenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-chloro-3-fluorobenzoyl)-1H-indol-3-yl]acetic acid;
- 25   methyl [6-chloro-2-(4-cyanobenzoyl)-1H-indol-3-yl]acetate;  
methyl [6-chloro-2-[4-bromobenzoyl]-1H-indol-3-yl]acetate;  
methyl [6-chloro-2-[4-(2-thienyl)benzoyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[4-(2-thienyl)benzoyl]-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[4-(2-furyl)benzoyl]-1H-indol-3-yl]acetate;
- 30   [6-chloro-2-[4-(2-furyl)benzoyl]-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[4-(3-pyridyl)benzoyl]-1H-indol-3-yl]acetate;

- [6-chloro-2-[4-(3-pyridyl)benzoyl]-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[4-(2-thiazolyl)benzoyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[4-(2-thiazolyl)benzoyl]-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(3-bromobenzoyl)-1H-indol-3-yl]acetate;
- 5 methyl [6-chloro-2-[3-(2-furyl)benzoyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[3-(2-furyl)benzoyl]-1H-indol-3-yl]acetic acid;  
methyl *dl*-2-[6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]propionate;  
*dl*-2-[2-(4-chlorobenzoyl)-6-chloro-1H-indol-3-yl]propionic acid;  
methyl [5-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetate;
- 10 [5-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(5-methylisoxazole-3-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(5-methylisoxazole-3-carbonyl)-1H-indol-3-yl]acetic acid;
- 15 methyl [6-chloro-2-(5-methylisoxazole-3-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(5-methylisoxazole-3-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-methyl-1,2,3-thiadiazole-5-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-methyl-1,2,3-thiadiazole-5-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-methyl-1,2,3-thiadiazole-5-carbonyl)-1H-indol-3-yl]acetate.
- 20 [6-chloro-2-(4-methyl-1,2,3-thiadiazole-5-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 25 [6-chloro-2-(2-thienyl)carbonylindol-3-yl]acetic acid;  
methyl [6-chloro-2-[3-(1-hydroxy-1-methylethyl)-2-furoyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[3-(1-hydroxy-1-methylethyl)-2-furoyl]-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[3-methoxymethyl-2-furoyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[3-methoxymethyl-2-furoyl]-1H-indol-3-yl]acetic acid;
- 30 [6-chloro-2-(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetate;

- methyl [5-chloro-2-(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(imidazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(imidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 5    methyl [6-chloro-2-(imidazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(imidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(1-methylpyrrole-2-carbonyl)-1H-indol-3-yl]acetate;
- 10   [5-chloro-2-(1-methylpyrrole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(2-methylimidazole-4-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(2-methylimidazole-4-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(thiazole-5-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(thiazole-5-carbonyl)-1H-indol-3-yl]acetic acid;
- 15   methyl [6-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-[3-(ethoxycaronyl)isoxazole-5-carbonyl]-1H-indol-3-yl]acetate;  
[5-chloro-2-[3-(carboxy)isoxazole-5-carbonyl]-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-cyclopropanecarbonyl-1H-indol-3-yl]acetate;
- 20   [6-chloro-2-cyclopropanecarbonyl-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-cyclobutanecarbonyl-1H-indol-3-yl]acetate;  
[6-chloro-2-cyclobutanecarbonyl-1H-indol-3-yl]acetic acid;  
methyl [5-(*tert*-butyl)-2-(4-chlorobenzoyl)-1H-indol-3-yl] acetate;  
[5-(*tert*-butyl)-2-(4-chlorobenzoyl)-1H-indol-3-yl] acetic acid;
- 25   [6-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]-*N,N*-dimethylacetamide;  
[6-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]-*N*-methylacetamide;  
[5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]-*N*-(2-hydroxyethyl)acetamide  
e;  
[5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]-*N*-methoxyacetamide;
- 30   2-[5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]-1-piperazinyl-1-ethanone;  
[5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]-*N*-(2-aminoethyl)acetamide;

- 2-[5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]-1-(3-amino-1-pyridinyl)-1-ethanone;
- [6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;
- methyl [6-chloro-5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 5 [6-chloro-5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- methyl [6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;
- [6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;
- [6-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- [6-chloro-2-(2-nitrobenzoyl)-1H-indol-3-yl]acetic acid;
- 10 [6-chloro-2-(2,4-dimethoxybenzoyl)-1H-indol-3-yl]acetic acid;
- [6-chloro-2-(4-difluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;
- [6-chloro-2-(2,5-dimethoxybenzoyl)-1H-indol-3-yl]acetic acid;
- methyl [5-acetyl-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetate;
- [5-acetyl-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;
- 15 methyl [6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetate;
- methyl [6-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- [6-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- methyl [6-fluoro-2-(4-chlorobenzoyl)-1H-indol-3-yl] acetate;
- [6-fluoro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;
- 20 [2-(4-methylpyridine-2-carbonyl)-5-methylthio-1H-indol-3-yl]acetic acid;
- [2-(4-methylpyridine-2-carbonyl)-5-methylthio-1H-indol-3-yl]acetic acid, and a salt thereof.
11. A compound according to claim 10 selected from
- ethyl (2-benzoyl-6-chloro-1H-indol-3-yl)acetate;
- 25 (2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid;
- (2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid, sodium salt;
- [6-chloro-2-(2-methylbenzoyl)-1H-indol-3-yl]acetic acid;
- [6-chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid;
- [6-chloro-2-(4-methylbenzoyl)-1H-indol-3-yl]acetic acid;
- 30 [6-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;
- methyl [6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetate;

- [6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-fluorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-fluorobenzoyl)-1H-indol-3-yl]acetic acid;  
[2-(3-bromobenzoyl)-6-chloro-1H-indol-3-yl]acetic acid;
- 5 [2-(4-bromobenzoyl)-6-chloro-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-trifluoromethylbenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-trifluoromethylbenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3,4-dichlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[2-benzoyl-4-chloro-1H-indol-3-yl]acetic acid;
- 10 [5-chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
[2-(3-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;
- 15 [5-methoxy-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
[2-benzoyl-7-chloro-1H-indol-3-yl]acetic acid;  
[2-benzoyl-4,5-dichloro-1H-indol-3-yl]acetic acid;  
[2-benzoyl-4,6-dichloro-1H-indol-3-yl]acetic acid;  
[2-benzoyl-5,6-dichloro-1H-indol-3-yl]acetic acid;
- 20 *dl*-2-(2-benzoyl-6-chloro-1H-indol-3-yl)propanoic acid;  
less polar antipode, 2-(2-benzoyl-6-chloro-1H-indol-3-yl)propanoic acid;  
more polar antipode, 2-(2-benzoyl-6-chloro-1H-indol-3-yl)propanoic acid;  
[6-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 25 methyl [6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(pyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 30 [5-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;

- methyl [5-chloro-2-(thiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(thiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl (2-benzoyl-6-chloro-1H-indol-3-yl)acetate;  
[2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;
- 5 [6-chloro-2-(2-furylcarbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(cyclohexanecarbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 10 [6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 15 [5-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[2-(4-*tert*-butylpyridine-2-carbonyl)-6-chloro-1H-indol-3-yl]acetic acid;  
[2-(4-*tert*-butylpyridine-2-carbonyl)-5-chloro-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(3-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 20 [6-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
[5-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 25 [6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(pyridine-3-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(pyridine-4-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-[4-(hydroxymethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;
- 30 [5-chloro-2-[4-(hydroxymethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(3,4-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;

- [5-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 5 [6-chloro-2-(3,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-ethoxy-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 10 [5-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5,6-dichloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 15 [5-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-ethyl-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 20 [5-isopropyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[2-(4-methylpyridine-2-carbonyl)-6-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[5-*tert*-butyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[2-(4-methyl-2-pyridine-2-carbonyl)-5-trifluoromethoxy-1H-indol-3-yl]acetic acid;  
[2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethoxy-1H-indol-3-yl]acetic acid;
- 25 [6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[2-(4-methylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
(2-benzoyl-1H-indol-3-yl)acetic acid;  
[2-(4-chlorobenzoyl)-6-methyl-1H-indol-3-yl]acetic acid;
- 30 [2-(4-chlorobenzoyl)-5-methyl-1H-indol-3-yl]acetic acid;  
[6-methoxy-2-(4-chlorobenzoyl)-1H-indol-3-yl] acetic acid;

- [2-(4-chlorobenzoyl)-6-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-ethyl-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-methoxy-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-isopropyl-1H-indol-3-yl]acetic acid;
- 5 [2-(4-chlorobenzoyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-trifluoromethoxy-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(2-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-benzyloxybenzoyl)-1H-indol-3-yl]acetic acid;
- 10 [6-chloro-2-(3-hydroxybenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-benzyloxybenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-hydroxybenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-isopropoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-phenylbenzoyl)-1H-indol-3-yl]acetic acid;
- 15 [6-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-nitrobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-[(4-methylsulfonyl)benzoyl]-1H-indol-3-yl]acetic acid;
- 20 [6-chloro-2-[4-(methylsulfonylamino)benzoyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(2-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(2,4-dichlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-chloro-3-fluorobenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-cyanobenzoyl)-1H-indol-3-yl]acetate;
- 25 methyl [6-chloro-2-[4-bromobenzoyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[4-(2-thienyl)benzoyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-[4-(2-furyl)benzoyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-[4-(3-pyridyl)benzoyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-[4-(2-thiazolyl)benzoyl]-1H-indol-3-yl]acetic acid;
- 30 methyl [6-chloro-2-(3-bromobenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-[3-(2-furyl)benzoyl]-1H-indol-3-yl]acetic acid;

- dl*-2-[2-(4-chlorobenzoyl)-6-chloro-1H-indol-3-yl]propionic acid;  
[5-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(5-methylisoxazole-3-carbonyl)-1H-indol-3-yl]acetic acid;
- 5 [6-chloro-2-(5-methylisoxazole-3-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methyl-1,2,3-thiadiazole-5-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-methyl-1,2,3-thiadiazole-5-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 10 [6-chloro-2-(2-thienyl)carbonylindol-3-yl]acetic acid;  
[6-chloro-2-[3-(1-hydroxy-1-methylethyl)-2-furoyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-[3-methoxymethyl-2-furoyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetate;
- 15 [5-chloro-2(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(imidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(imidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(1-methylpyrrole-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 20 [5-chloro-2-(2-methylimidazole-4-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(thiazole-5-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-[3-(carboxy)isoxazole-5-carbonyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-cyclopropanecarbonyl-1H-indol-3-yl]acetic acid;
- 25 [6-chloro-2-cyclobutanecarbonyl-1H-indol-3-yl]acetic acid;  
[5-(*tert*-butyl)-2-(4-chlorobenzoyl)-1H-indol-3-yl] acetic acid;  
[6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
[6-chloro-5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;
- 30 [6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-ethyl-3-fluoro-pyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;

- [6-chloro-2-(2-nitrobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(2,4-dimethoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-difluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(2,5-dimethoxybenzoyl)-1H-indol-3-yl]acetic acid;
- 5 [5-acetyl-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid, and a salt thereof.
12. A compound according to claim 10 selected from  
ethyl (2-benzoyl-6-chloro-1H-indol-3-yl)acetate;  
(2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid;  
[6-chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid;
- 10 [6-chloro-2-(4-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-fluorobenzoyl)-1H-indol-3-yl]acetic acid;
- 15 [6-chloro-2-(4-fluorobenzoyl)-1H-indol-3-yl]acetic acid;  
[2-(3-bromobenzoyl)-6-chloro-1H-indol-3-yl]acetic acid;  
[2-(4-bromobenzoyl)-6-chloro-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-trifluoromethylbenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-trifluoromethylbenzoyl)-1H-indol-3-yl]acetic acid;
- 20 (2-benzoyl-4-chloro-1H-indol-3-yl)acetic acid;  
[5-chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;
- 25 [2-(3-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
(2-benzoyl-4,5-dichloro-1H-indol-3-yl)acetic acid;  
(2-benzoyl-4,6-dichloro-1H-indol-3-yl)acetic acid;  
(2-benzoyl-5,6-dichloro-1H-indol-3-yl)acetic acid;  
*dl*-2-(2-benzoyl-6-chloro-1H-indol-3-yl)propanoic acid;
- 30 less polar antipode, 2-(2-benzoyl-6-chloro-1H-indol-3-yl)propanoic acid;  
more polar antipode, 2-(2-benzoyl-6-chloro-1H-indol-3-yl)propanoic acid;

- [6-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 5 [6-chloro-2-(pyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 10 methyl [5-chloro-2-(thiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(thiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl (2-benzoyl-6-chloro-1H-indol-3-yl)acetate;  
[6-chloro-2-(2-furylcarbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(cyclohexanecarbonyl)-1H-indol-3-yl]acetic acid;
- 15 methyl [6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 20 [5-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 25 methyl [5-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [2-(4-*tert*-butylpyridine-2-carbonyl)-6-chloro-1H-indol-3-yl]acetate;  
[2-(4-*tert*-butylpyridine-2-carbonyl)-6-chloro-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(3-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 30 [6-chloro-2-(3-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;

- [6-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;
- 5 [6-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;  
[5-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 10 methyl [6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-[4-(hydroxymethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate.
- 15 [5-chloro-2-[4-(hydroxymethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 20 methyl [6-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(3,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 25 [6-chloro-2-(3,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(3-ethoxy-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 30 methyl [6-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;

- methyl [5-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 5   methyl [6-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5,6-dichloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5,6-dichloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 10   [5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 15   methyl [6-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-ethyl-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 20   [5-ethyl-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-isopropyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-isopropyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 25   methyl [2-(4-methylpyridine-2-carbonyl)-6-trifluoromethyl-1H-indol-3-yl]acetate;  
[2-(4-methylpyridine-2-carbonyl)-6-trifluoromethyl-1H-indol-3-yl]acetic acid;  
methyl [5-*tert*-butyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-*tert*-butyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [2-(4-methylpyridine-2-carbonyl)-5-trifluoromethoxy-1H-indol-3-yl]acetate;
- 30   [2-(4-methyl-2-pyridine-2-carbonyl)-5-trifluoromethoxy-1H-indol-3-yl]acetic acid;  
methyl [6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;

- [6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [2-(4-methylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetate;  
[2-(4-methylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
methyl [2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetate;
- 5 [2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
methyl [2-(4-chlorobenzoyl)-6-methyl-1H-indol-3-yl]acetate;  
[2-(4-chlorobenzoyl)-6-methyl-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-methyl-1H-indol-3-yl]acetic acid;  
methyl [2-(4-chlorobenzoyl)-5-trifluoromethyl-1H-indol-3-yl]acetate;
- 10 [2-(4-chlorobenzoyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
methyl [2-(4-chlorobenzoyl)-5-trifluoromethoxy-1H-indol-3-yl] acetate;  
[2-(4-chlorobenzoyl)-5-trifluoromethoxy-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(3-methoxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(3-methoxybenzoyl)-1H-indol-3-yl]acetic acid;
- 15 methyl [6-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetate;
- 20 [5-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[4-(2-furyl)benzoyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[4-(2-furyl)benzoyl]-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;
- 25 methyl [6-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(5-methylisoxazole-3-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(5-methylisoxazole-3-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate;
- 30 [5-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate;

- [6-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[3-methoxymethyl-2-furoyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[3-methoxymethyl-2-furoyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 5    methyl [5-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(2-methylimidazole-4-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(2-methylimidazole-4-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate;
- 10   [6-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 15   methyl [6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetate, and a salt thereof.
13. A compound according to claim 10 selected from  
ethyl (2-benzoyl-6-chloro-1H-indol-3-yl)acetate;  
(2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid;  
[6-chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid;
- 20   [6-chloro-2-(4-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-fluorobenzoyl)-1H-indol-3-yl]acetic acid;
- 25   [6-chloro-2-(4-fluorobenzoyl)-1H-indol-3-yl]acetic acid;  
[2-(3-bromobenzoyl)-6-chloro-1H-indol-3-yl]acetic acid;  
[2-(4-bromobenzoyl)-6-chloro-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-trifluoromethylbenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-trifluoromethylbenzoyl)-1H-indol-3-yl]acetic acid;
- 30   (2-benzoyl-4-chloro-1H-indol-3-yl)acetic acid;  
[5-chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid;

- [5-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
[2-(3-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;
- 5 (2-benzoyl-4,5-dichloro-1H-indol-3-yl)acetic acid;  
(2-benzoyl-4,6-dichloro-1H-indol-3-yl)acetic acid;  
(2-benzoyl-5,6-dichloro-1H-indol-3-yl)acetic acid;  
*dl*-2-(2-benzoyl-6-chloro-1H-indol-3-yl)propanoic acid;  
less polar antipode, 2-(2-benzoyl-6-chloro-1H-indol-3-yl)propanoic acid;
- 10 more polar antipode, 2-(2-benzoyl-6-chloro-1H-indol-3-yl)propanoic acid;  
[6-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 15 [6-chloro-2-(pyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 20 methyl [5-chloro-2-(thiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(thiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl (2-benzoyl-6-chloro-1H-indol-3-yl)acetate;  
[6-chloro-2-(2-furylcarbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(cyclohexanecarbonyl)-1H-indol-3-yl]acetic acid;
- 25 methyl [6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 30 [6-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;

- [5-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[2-(4-*tert*-butylpyridine-2-carbonyl)-6-chloro-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 5 [5-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
[5-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 10 [5-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-[4-(hydroxymethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 15 [5-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-ethoxy-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 20 [5-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5,6-dichloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 25 [5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-methoxy-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-ethyl-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 30 [6-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-isopropyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;

- [2-(4-methylpyridine-2-carbonyl)-6-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[5-*tert*-butyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[2-(4-methyl-2-pyridine-2-carbonyl)-5-trifluoromethoxy-1H-indol-3-yl]acetic acid;  
[6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 5 [2-(4-methylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-6-methyl-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-methyl-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;
- 10 [2-(4-chlorobenzoyl)-5-trifluoromethoxy-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;
- 15 [6-chloro-2-[4-(2-furyl)benzoyl]-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(5-methylisoxazole-3-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 20 [6-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-[3-methoxymethyl-2-furoyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(1-methylimidazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(2-methylimidazole-4-carbonyl)-1H-indol-3-yl]acetic acid;
- 25 [6-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
2-[6-chloro-2-[(4-ethyl-3-fluoro-2-pyridinyl)carbonyl]-1H-indol-3-yl]acetic acid;
- 30 methyl [6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetate, and a salt thereof.
14. A compound according to claim 10 selected from

- (2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid;  
[6-chloro-2-(4-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetate;
- 5 [6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-fluorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-fluorobenzoyl)-1H-indol-3-yl]acetic acid;  
[2-(3-bromobenzoyl)-6-chloro-1H-indol-3-yl]acetic acid;  
[2-(4-bromobenzoyl)-6-chloro-1H-indol-3-yl]acetic acid;
- 10 [6-chloro-2-(4-trifluoromethylbenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;
- 15 [2-(3-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
(2-benzoyl-4,5-dichloro-1H-indol-3-yl)acetic acid;  
(2-benzoyl-4,6-dichloro-1H-indol-3-yl)acetic acid;  
(2-benzoyl-5,6-dichloro-1H-indol-3-yl)acetic acid;  
[6-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 20 [6-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(pyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 25 methyl [5-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(thiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(thiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl (2-benzoyl-6-chloro-1H-indol-3-yl)acetate;
- 30 [6-chloro-2-(cyclohexanecarbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetate;

- [6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 5 [5-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 10 methyl [6-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate.
- 15 [6-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;  
[5-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 20 methyl [6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 25 [5-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 30 methyl [5-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;

- methyl [6-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(3-ethoxy-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 5    methyl [5-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5,6-dichloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 10   10   [5,6-dichloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 15   15   methyl [5-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-isopropyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-isopropyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [2-(4-methylpyridine-2-carbonyl)-6-trifluoromethyl-1H-indol-3-yl]acetate;
- 20   20   [2-(4-methylpyridine-2-carbonyl)-6-trifluoromethyl-1H-indol-3-yl]acetic acid;  
methyl [5-*tert*-butyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-*tert*-butyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [2-(4-methylpyridine-2-carbonyl)-5-trifluoromethoxy-1H-indol-3-yl]acetate;  
[2-(4-methyl-2-pyridine-2-carbonyl)-5-trifluoromethoxy-1H-indol-3-yl]acetic acid;
- 25   25   methyl [6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [2-(4-methylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetate;  
[2-(4-methylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
methyl [2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetate;
- 30   30   [2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-methyl-1H-indol-3-yl]acetic acid;

- methyl [2-(4-chlorobenzoyl)-5-trifluoromethyl-1H-indol-3-yl]acetate;  
[2-(4-chlorobenzoyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;
- 5   methyl [5-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[4-(2-furyl)benzoyl]-1H-indol-3-yl]acetate;
- 10   [6-chloro-2-[4-(2-furyl)benzoyl]-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;
- 15   methyl [5-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[3-methoxymethyl-2-furoyl]-1H-indol-3-yl]acetate;
- 20   [6-chloro-2-[3-methoxymethyl-2-furoyl]-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(2-methylimidazole-4-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(2-methylimidazole-4-carbonyl)-1H-indol-3-yl]acetic acid;
- 25   methyl [6-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetate, and a salt thereof.
- 30       15. A compound according to claim 10 selected from  
(2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid;

- [6-chloro-2-(4-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;
- 5 [6-chloro-2-(3-fluorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-fluorobenzoyl)-1H-indol-3-yl]acetic acid;  
[2-(3-bromobenzoyl)-6-chloro-1H-indol-3-yl]acetic acid;  
[2-(4-bromobenzoyl)-6-chloro-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-trifluoromethylbenzoyl)-1H-indol-3-yl]acetic acid;
- 10 [5-chloro-2-(3-methylbenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
[2-(3-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;
- 15 (2-benzoyl-4,5-dichloro-1H-indol-3-yl)acetic acid;  
(2-benzoyl-4,6-dichloro-1H-indol-3-yl)acetic acid;  
(2-benzoyl-5,6-dichloro-1H-indol-3-yl)acetic acid;  
[6-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 20 methyl [6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(pyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 25 [5-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(thiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(thiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl (2-benzoyl-6-chloro-1H-indol-3-yl)acetate;  
[6-chloro-2-(cyclohexanecarbonyl)-1H-indol-3-yl]acetic acid;
- 30 methyl [6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;

- methyl [6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 5 [6-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(6-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
[5-chloro-2-[5-(trifluoromethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;
- 10 [5-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4,5-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 15 [6-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-ethoxy-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(3-chloro-4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 20 [6-chloro-2-(4,6-dimethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5,6-dichloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-ethyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 25 [5-isopropyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[2-(4-methylpyridine-2-carbonyl)-6-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[5-*tert*-butyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[2-(4-methyl-2-pyridine-2-carbonyl)-5-trifluoromethoxy-1H-indol-3-yl]acetic acid;  
[6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 30 [2-(4-methylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;

- [2-(4-chlorobenzoyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-trifluoromethoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;
- 5 [6-chloro-2-[4-(2-furyl)benzoyl]-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(5-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 10 [6-chloro-2-[3-methoxymethyl-2-furoyl]-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(2-methylimidazole-4-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-methylthiazole-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;
- 15 [6-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetate;  
[6-chloro-5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid,
- 20 and a salt thereof.
16. A compound according to claim 1 selected from  
(2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid;  
[6-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;
- 25 [5-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
(2-benzoyl-5,6-dichloro-1H-indol-3-yl)acetic acid;  
[6-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 30 [6-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;

- [6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(pyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 5    methyl [5-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 10    [6-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetate;  
[2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;
- 15    methyl [6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 20    [6-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetatic acid;  
methyl [5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 25    methyl [5-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 30    methyl [6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetate;  
[6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;

- [6-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetate;  
[6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate;
- 5 [6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
methyl [5-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetate;  
[5-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid (cj-020,099);  
methyl [6-chloro-5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetate,
- 10 and a salt thereof.
17. A compound according to claim 10 selected from  
(2-benzoyl-6-chloro-1H-indol-3-yl)acetic acid;  
[6-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;
- 15 [5-chloro-2-(4-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(3-chlorobenzoyl)-1H-indol-3-yl]acetic acid;  
[2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid;  
(2-benzoyl-5,6-dichloro-1H-indol-3-yl)acetic acid;  
[6-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 20 [6-chloro-2-(5-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(pyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 25 [6-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-ethylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-isopropylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-propylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 30 [5-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[2-(4-ethylpyridine-2-carbonyl)-5-trifluoromethyl-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;

- [6-chloro-2-(4-methoxypyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-fluoro-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[5-chloro-2-(4-methoxybenzoyl)-1H-indol-3-yl]acetic acid;
- 5 [6-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-[4-(1-hydroxyethyl)pyridine-2-carbonyl]-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-ethyl-3-fluoropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(5-chloropyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-methyl-2-(4-methylpyridine-2-carbonyl)-1H-indol-3-yl]acetic acid;
- 10 [5-chloro-2-(isoquinoline-3-carbonyl)-1H-indol-3-yl]acetic acid;  
[6-chloro-2-(4-chlorobenzoyl)-5-fluoro-1H-indol-3-yl]acetic acid,  
and a salt thereof.
18. A pharmaceutical composition useful for the treatment of a medical condition in which prostaglandins are implicated as pathogens, which comprises a compound of the formula (I) of claim 1, and a pharmaceutically inert carrier.
- 15 19. A pharmaceutical composition according to claim 18, wherein the compound of the formula (I) is as defined in Claim 2.
20. A pharmaceutical composition according to claim 19, wherein the compound of the formula (I) is as defined in Claim 3.
- 20 21. A pharmaceutical composition according to claim 20, wherein the compound of the formula (I) is as defined in Claim 4.
22. A pharmaceutical composition according to claim 21, wherein the compound of the formula (I) is as defined in Claim 5.
- 25 23. A pharmaceutical composition according to claim 22, wherein the compound of the formula (I) is as defined in Claim 6.
24. A pharmaceutical composition according to claim 23, wherein the compound is as defined in Claim 7.
- 25 25. A pharmaceutical composition according to claim 24, wherein the compound is as defined in Claim 8.
- 30 26. A pharmaceutical composition according to claim 25, wherein the compound is as defined in Claim 9.

27. A pharmaceutical composition according to claim 26, wherein the compound is as defined in Claim 10.

28. A pharmaceutical composition according to claim 27, wherein the compound is as defined in Claim 11.

5 29. A pharmaceutical composition according to claim 28, wherein the compound is as defined in Claim 12.

30. A pharmaceutical composition according to claim 29, wherein the compound is as defined in Claim 13.

10 31. A pharmaceutical composition according to claim 30, wherein the compound is as defined in Claim 14.

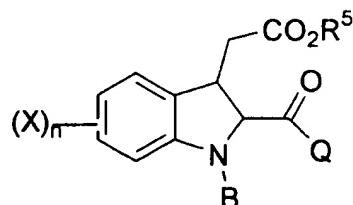
32. A pharmaceutical composition according to claim 31, wherein the compound is as defined in Claim 15.

33. A pharmaceutical composition according to claim 32, wherein the compound is as defined in Claim 16.

15 34. A pharmaceutical composition according to claim 33, wherein the compound is as defined in Claim 17.

35. A method for the treatment of a medical condition in which prostaglandins are implicated as pathogens, in a mammalian subject, which comprises administering to said pharmaceutical composition according to claim 1.

20 36. A compound of the formula:



7-VI

wherein **B** is a suitable protecting group;

**Q** is selected from the following:

25 (a) phenyl optionally substituted with one, two or three substituents independently selected from

- (a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>R<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub>-cycloalkyl,
- 5 (a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
- 10 (a-3) 5-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
- 15 (a-4) 6-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
- 20 (b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),
- 25 (c) a 5-membered monocyclic aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);
- 30

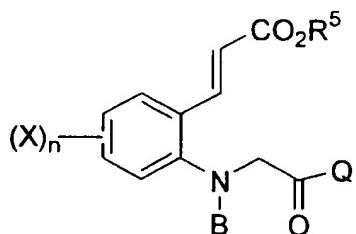
- (d)  $C_{3-7}$  cycloalkyl optionally substituted with one or two substituents independently selected from OH,  $C_{1-4}$  alkyl, halo and halo-substituted  $C_{1-4}$  alkyl; and
- (e) a benzo-fuzed heterocycle optionally substituted with one, two or three substituents independently selected from the group (a-1);

5  $R^2$  and  $R^3$  are independently H, OH,  $C_{1-4}$  alkoxy,  $C_{1-4}$  alkyl or  $C_{1-4}$  alkyl substituted with halo, OH,  $C_{1-4}$  alkoxy,  $NH_2$  or  $CN$ ;

10  $X$  is independently selected from halo,  $C_{1-4}$  alkyl, halo-substituted  $C_{1-4}$  alkyl, OH,  $C_{1-4}$  alkoxy, halo-substituted  $C_{1-4}$  alkoxy,  $C_{1-4}$  alkylthio,  $NO_2$ ,  $NH_2$ , di-( $C_{1-4}$  alkyl)amino,  $C_{1-4}$  alkylamino,  $CN$ ,  $HO-(C_{1-4})$  alkyl,  $C_{1-4}$  alkoxy- $C_{1-4}$  alkyl,  $C_{1-4}$  alkylsulfonyl, aminosulfonyl,  $-NH_2S(O)_2NR^2R^3$ , acetyl,  $-COOH$ ,  $-C(O)O-C_{1-4}$  alkyl,  $C_{1-4}$  alkylsulfonylamino and  $C_{3-7}$  cycloalkyl;  $R^5$  is  $C_{1-6}$  alkyl; and

15  $n$  is 0, 1, 2, 3 or 4.

37. A compound of the formula:



15

7-V

wherein  $B$  is a suitable protecting group;

$Q$  is selected from the following:

- (a) phenyl optionally substituted with one, two or three substituents independently selected from
- 20 (a-1) halo,  $C_{1-4}$  alkyl, halo-substituted  $C_{1-4}$  alkyl, OH,  $C_{1-4}$  alkoxy, halo-substituted  $C_{1-4}$  alkoxy,  $C_{1-4}$  alkylthio,  $NO_2$ ,  $NH_2$ , di-( $C_{1-4}$  alkyl)amino,  $C_{1-4}$  alkylamino,  $CN$ ,  $HO-(C_{1-4})$  alkyl,  $C_{1-4}$  alkoxy- $C_{1-4}$  alkyl,  $C_{1-4}$  alkylsulfonyl, aminosulfonyl,  $-NH_2S(O)_2NR^2R^3$ , acetyl,  $-COOH$ ,  $-C(O)O-C_{1-4}$  alkyl,  $C_{1-4}$  alkylsulfonylamino and  $C_{3-7}$  cycloalkyl,

- (a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
- 5 (a-3) 5-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
- 10 (a-4) 6-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
- 15 (b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),
- 20 (c) a 5-membered monocyclic aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);
- 25 (d) C<sub>3-7</sub> cycloalkyl optionally substituted with one or two substituents independently selected from OH, C<sub>1-4</sub> alkyl, halo and halo-substituted C<sub>1-4</sub> alkyl; and
- (e) a benzo-fused heterocycle optionally substituted with one, two or three substituents independently selected from the group (a-1);
- 30

R<sup>2</sup> and R<sup>3</sup> are independently H, OH, C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkyl substituted

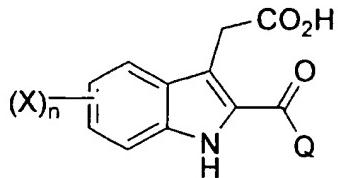
with halo, OH, C<sub>1-4</sub> alkoxy, NH<sub>2</sub> or CN;

X is independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl,

5 aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>R<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl; R<sup>5</sup> is C<sub>1-6</sub> alkyl; and

n is 0, 1, 2, 3 or 4.

38. A process for preparing a compound of the formula:



7-IV

10 wherein

Q is selected from the following:

(a) phenyl optionally substituted with one, two or three substituents independently selected from

(a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>R<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl,

15

(a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

20

(a-3) 5-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-

25

one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-

substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

(a-4) 6-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

(b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),

(c) a 5-membered monocyclic aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);

(d) C<sub>3-7</sub> cycloalkyl optionally substituted with one or two substituents independently selected from OH, C<sub>1-4</sub> alkyl, halo and halo-substituted C<sub>1-4</sub> alkyl; and

(e) a benzo-fuzed heterocycle optionally substituted with one, two or three substituents independently selected from the group (a-1);

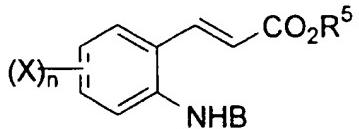
R<sup>2</sup> and R<sup>3</sup> are independently H, OH, C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkyl substituted with halo, OH, C<sub>1-4</sub> alkoxy, NH<sub>2</sub> or CN;

X is independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>NR<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl; and

n is 0, 1, 2, 3 or 4,

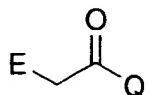
which process comprises the steps of:

- i) reacting a compound of the formula:



**7-II**

wherein B is a suitable protecting group; R<sup>5</sup> is C<sub>1-6</sub> alkyl; X and n are as defined above, with a compound of the formula:



wherein E is halo and Q are as defined above, with a first base and a suitable solvent;

- ii) reacting the product of step i) with a second base.
- iii) reacting the product of step ii) with an acid.

10 39. The process according to claim 38, wherein said first base is potassium carbonate, potassium bicarbonate, sodium bicarbonate, sodium carbonate or cesium carbonate.

40. The process according to claim 38, wherein said first base is potassium carbonate.

15 41. The process according to claim 38, wherein said second base is aqueous sodium hydroxide, potassium hydroxide, sodium carbonate, potassium carbonate, sodium pentoxide (followed by water), sodium methoxide (followed by water) or potassium *t*-butoxide (followed by water).

42. The process according to claim 38, wherein said second base is sodium 20 hydroxide.

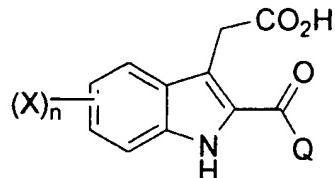
43. The process according to claim 38, wherein said acid is aqueous hydrochloric acid, hydrobromic acid, sulfuric acid or ammonium chloride.

44. The process according to claim 38, wherein said acid is aqueous hydrochloric acid.

25 45. The process according to claim 38, wherein said solvent is *N,N*-dimethylacetamide, *N,N*-dimethylformamide, methyl ethyl ketone, acetone, or tetrahydrofuran.

46. The process according to claim 38, wherein said solvent is N,N-dimethylacetamide.

47. A process for preparing a compound of the formula:



### 7-IV

5 wherein

**Q** is selected from the following:

- (a) phenyl optionally substituted with one, two or three substituents independently selected from
  - (a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>R<sup>3</sup>, acetyl-COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>1-4</sub> cycloalkyl,
  - (a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
  - (a-3) 5-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
  - (a-4) 6-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-

substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

- 5 (b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),

10 (c) a 5-membered monocyclic aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);

15 (d) C<sub>3-7</sub> cycloalkyl optionally substituted with one or two substituents independently selected from OH, C<sub>1-4</sub> alkyl, halo and halo-substituted C<sub>1-4</sub> alkyl; and

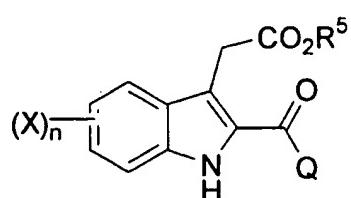
(e) a benzo-fuzed heterocycle optionally substituted with one, two or three substituents independently selected from the group (a-1);

**R<sup>2</sup>** and **R<sup>3</sup>** are independently H, OH, C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkyl substituted with halo, OH, C<sub>1-4</sub> alkoxy, NH<sub>2</sub> or CN;

- 20 X is independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>NR<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl; and

25 n is 0, 1, 2, 3 or 4.

which process comprises reacting a compound of the formula:



wherein R<sup>5</sup> is C<sub>1-6</sub> alkyl; Q, X and n are as defined as before, with a base in a suitable solvent.

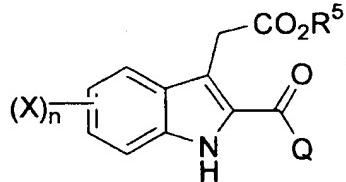
48. The process according to claim 47, wherein said base is sodium hydroxide, potassium hydroxide, sodium carbonate, potassium carbonate, sodium bicarbonate, potassium bicarbonate, sodium t-pentoxide, sodium methoxide, sodium ethoxide or potassium t-butoxide.

49. The process according to claim 47, wherein said base is sodium hydroxide.

50. The process according to claim 47, wherein said solvent is an aqueous mixture of methanol, ethanol, isopropyl alcohol or tetrahydrofuran.

51. The process according to claim 47, wherein said solvent is methanol containing water.

52. A process of preparing a compound of the formula:



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15

wherein

Q is selected from the following:

(a) phenyl optionally substituted with one, two or three substituents independently selected from

20 (a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-12</sub> cycloalkyl,

25 (a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally substituted with one, two or three substituents independently

selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

(a-3) 5-membered monocyclic aromatic group optionally substituted with

5 one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

(a-4) 6-membered monocyclic aromatic group optionally substituted with

10 one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

(b) a 6-membered monocyclic aromatic group containing one, two, three or 15 four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),

(c) a 5-membered monocyclic aromatic group containing one heteroatom 20 selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);

(d) C<sub>3-7</sub> cycloalkyl optionally substituted with one or two substituents 25 independently selected from OH, C<sub>1-4</sub> alkyl, halo and halo-substituted C<sub>1-4</sub> alkyl; and

(e) a benzo-fuzed heterocycle optionally substituted with one, two or three substituents independently selected from the group (a-1);

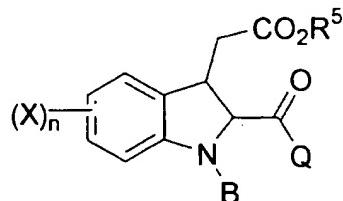
R<sup>2</sup> and R<sup>3</sup> are independently H, OH, C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkyl substituted 30 with halo, OH, C<sub>1-4</sub> alkoxy, NH<sub>2</sub> or CN;

X is independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub>

alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkylamino)C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylaminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>NR<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl; R<sup>5</sup> is C<sub>1-6</sub> alkyl; and

5 n is 0, 1, 2, 3 or 4,

which process comprises reacting a compound of the formula:



7-VI

wherein B, Q, X, n and R<sup>5</sup> are as defined above with a base in a suitable solvent.

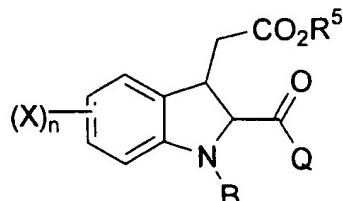
10 53. The process according to claim 52, wherein said base is 1,8-diazabicyclo[5.4.0]undec-7-ene, 1,5-diazabicyclo[4.3.0]non-5-ene, 1,1,3,3-tetramethylguanidine, sodium t-pentoxide, sodium methoxide, or potassium t-butoxide

54. The process according to claim 52, wherein said base is 1,8-diazabicyclo[5.4.0]undec-7-ene or potassium t-butoxide.

15 55. The process according to claim 52, wherein said solvent is N,N-dimethylacetamide, N,N-dimethylformamide, methyl ethyl ketone, acetone or tetrahydrofuran.

56. The process according to claim 52, wherein said solvent is N,N-dimethylacetamide.

20 57. A process for preparing a compound of the formula:



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wherein B is a suitable protecting group;

Q is selected from the following:

- (a) phenyl optionally substituted with one, two or three substituents independently selected from
- (a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>R<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl,
- (a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
- (a-3) 5-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
- (a-4) 6-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,
- (b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),
- (c) a 5-membered monocyclic aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic

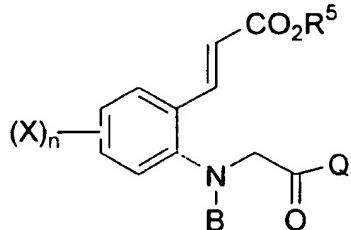
aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);

- 5           (d)  $C_{3-7}$  cycloalkyl optionally substituted with one or two substituents independently selected from OH,  $C_{1-4}$  alkyl, halo and halo-substituted  $C_{1-4}$  alkyl; and
- (e) a benzo-fuzed heterocycle optionally substituted with one, two or three substituents independently selected from the group (a-1);

$R^2$  and  $R^3$  are independently H, OH,  $C_{1-4}$  alkoxy,  $C_{1-4}$  alkyl or  $C_{1-4}$  alkyl substituted with halo, OH,  $C_{1-4}$  alkoxy,  $NH_2$  or CN;

10            $X$  is independently selected from halo,  $C_{1-4}$  alkyl, halo-substituted  $C_{1-4}$  alkyl, OH,  $C_{1-4}$  alkoxy, halo-substituted  $C_{1-4}$  alkoxy,  $C_{1-4}$  alkylthio,  $NO_2$ ,  $NH_2$ , di-( $C_{1-4}$  alkyl)amino,  $C_{1-4}$  alkylamino, CN,  $HO-(C_{1-4})$  alkyl,  $C_{1-4}$  alkoxy- $C_{1-4}$  alkyl,  $C_{1-4}$  alkylsulfonyl, aminosulfonyl,  $-NH_2S(O)_2NR^2NR^3$ , acetyl, -COOH,  $-C(O)O-C_{1-4}$  alkyl,  $C_{1-4}$  alkylsulfonylamino and  $C_{3-7}$  cycloalkyl;  $R^5$  is  $C_{1-6}$  alkyl; and

15           n is 0, 1, 2, 3 or 4,  
which process comprises reacting a compound of the formula:



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20           wherein B, Q, X, n and  $R^5$  are as defined above, with a base in the presence of a solvent.

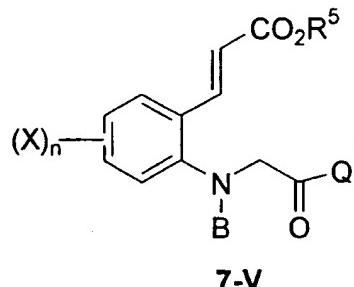
58.          The process according to claim 57, wherein said base is potassium carbonate, potassium bicarbonate, sodium bicarbonate, sodium carbonate, or cesium carbonate.

25          59.          The process according to claim 57, wherein said base is potassium carbonate.

60. The process according to claim 57, wherein said solvent is *N,N*-dimethylacetamide, *N,N*-dimethylformamide, methyl ethyl ketone, acetone, or tetrahydrofuran.

61. The process according to claim 57, wherein said solvent is *N,N*-dimethylacetamide.

62. A process for preparing a compound of the formula:



wherein **B** is a suitable protecting group;

10 **Q** is selected from the following:

(a) phenyl optionally substituted with one, two or three substituents independently selected from

(a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>R<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl,

(a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

(a-3) 5-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-

substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

(a-4) 6-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

(b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),

(c) a 5-membered monocyclic aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);

(d) C<sub>3-7</sub> cycloalkyl optionally substituted with one or two substituents independently selected from OH, C<sub>1-4</sub> alkyl, halo and halo-substituted C<sub>1-4</sub> alkyl; and

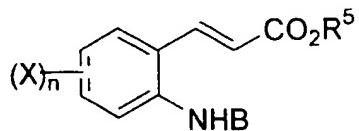
(e) a benzo-fused heterocycle optionally substituted with one, two or three substituents independently selected from the group (a-1);

R<sup>2</sup> and R<sup>3</sup> are independently H, OH, C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkyl substituted with halo, OH, C<sub>1-4</sub> alkoxy, NH<sub>2</sub> or CN;

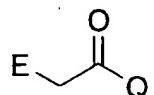
X is independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>NR<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl; R<sup>5</sup> is C<sub>1-6</sub> alkyl; and

n is 0, 1, 2, 3 or 4,

which comprises reacting a compound of the formula:



wherein B, X, n and R<sup>5</sup> are as defined above, with a compound of the formula:



wherein E is halo and Q are as defined above, with a base in the presence of a  
5 solvent.

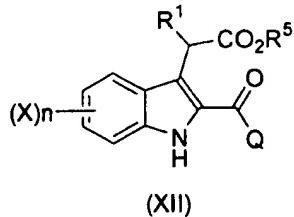
63. The process according to claim 62, wherein said base is potassium carbonate, potassium bicarbonate, sodium bicarbonate, sodium carbonate, or cesium carbonate.

64. The process according to claim 62, wherein said base is potassium  
10 carbonate.

65. The process according to claim 62, wherein said solvent is *N,N*-dimethylacetamide, *N,N*-dimethylformamide, methyl ethyl ketone, acetone or tetrahydrofuran.

66. The process according to claim 62, wherein said solvent is  
15 *N,N*-dimethylacetamide.

67. A process for preparing a compound of the formula (XII):



wherein

Q is selected from the following:

- 20 (a) phenyl optionally substituted with one, two or three substituents independently selected from  
 (a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-</sub>

$\text{C}_{1-4}$  alkyl,  $\text{C}_{1-4}$  alkylsulfonyl, aminosulfonyl,  $-\text{NH}_2\text{S}(\text{O})_2\text{NR}'\text{R}''$ , acetyl,  $-\text{COOH}$ ,  $-\text{C}(\text{O})\text{O}-\text{C}_{1-4}$  alkyl,  $\text{C}_{1-4}$  alkylsulfonylamino and  $\text{C}_{1-4}$  cycloalkyl,

(a-2) aryl or  $-\text{O}-(\text{CH}_2)_n\text{-aryl}$ , and the aryl or aryl moiety being optionally

5 substituted with one, two or three substituents independently selected from halo,  $\text{C}_{1-4}$  alkyl, halo-substituted  $\text{C}_{1-4}$  alkyl, OH,  $\text{C}_{1-4}$  alkoxy, halo-substituted  $\text{C}_{1-4}$  alkoxy,  $\text{C}_{1-4}$  alkylthio,  $\text{NO}_2$ ,  $\text{NH}_2$ , di- $(\text{C}_{1-4}$  alkyl)amino,  $\text{C}_{1-4}$  alkylamino and CN,

(a-3) 5-membered monocyclic aromatic group optionally substituted with

10 one, two or three substituents independently selected from halo,  $\text{C}_{1-4}$  alkyl, halo-substituted  $\text{C}_{1-4}$  alkyl, OH,  $\text{C}_{1-4}$  alkoxy, halo-substituted  $\text{C}_{1-4}$  alkoxy,  $\text{C}_{1-4}$  alkylthio,  $\text{NO}_2$ ,  $\text{NH}_2$ , di- $(\text{C}_{1-4}$  alkyl)amino,  $\text{C}_{1-4}$  alkylamino and CN,

(a-4) 6-membered monocyclic aromatic group optionally substituted with

15 one, two or three substituents independently selected from halo,  $\text{C}_{1-4}$  alkyl, halo-substituted  $\text{C}_{1-4}$  alkyl, OH,  $\text{C}_{1-4}$  alkoxy, halo-substituted  $\text{C}_{1-4}$  alkoxy,  $\text{C}_{1-4}$  alkylthio,  $\text{NO}_2$ ,  $\text{NH}_2$ , di- $(\text{C}_{1-4}$  alkyl)amino,  $\text{C}_{1-4}$  alkylamino and CN,

(b) a 6-membered monocyclic aromatic group containing one, two, three or 20 four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),

(c) a 5-membered monocyclic aromatic group containing one heteroatom 25 selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);

(d)  $\text{C}_{3-7}$  cycloalkyl optionally substituted with one or two substituents 30 independently selected from OH,  $\text{C}_{1-4}$  alkyl, halo and halo-substituted  $\text{C}_{1-4}$  alkyl; and

- (e) a benzo-fused heterocycle optionally substituted with one, two or three substituents independently selected from the group (a-1);

$R^1$  is hydrogen,  $C_{1-4}$  alkyl or halo;

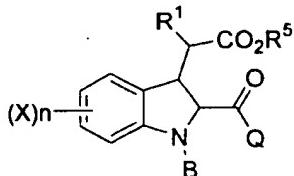
5  $R^2$  and  $R^3$  are independently H, OH,  $C_{1-4}$  alkoxy,  $C_{1-4}$  alkyl or  $C_{1-4}$  alkyl substituted with halo, OH,  $C_{1-4}$  alkoxy,  $NH_2$  or CN;

$R^5$  is  $C_{1-6}$  alkyl;

10  $X$  is independently selected from halo,  $C_{1-4}$  alkyl, halo-substituted  $C_{1-4}$  alkyl, OH,  $C_{1-4}$  alkoxy, halo-substituted  $C_{1-4}$  alkoxy,  $C_{1-4}$  alkylthio,  $NO_2$ ,  $NH_2$ , di-( $C_{1-4}$  alkyl)amino,  $C_{1-4}$  alkylamino, CN,  $HO-(C_{1-4})$  alkyl,  $C_{1-4}$  alkoxy- $C_{1-4}$  alkyl,  $C_{1-4}$  alkylsulfonyl, aminosulfonyl,  $-NH_2S(O)_2NR^2NR^3$ , acetyl,  $-COOH$ ,  $-C(O)O-C_{1-4}$  alkyl,  $C_{1-4}$  alkylsulfonylamino and  $C_{3-7}$  cycloalkyl; and

$n$  is 0, 1, 2, 3 or 4,

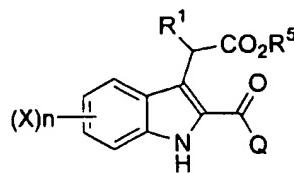
which process comprises treating a compound of the formula (X):



(X)

15 wherein  $R^1$ ,  $R^5$ ,  $X$ ,  $Q$  and  $n$  are as defined herein before, and  $B$  is a suitable protecting group, in the presence of a suitable base to obtain a compound of the formula (XII).

68. A process for preparing a compound of the formula (XII):



(XII)

wherein

20  $Q$  is selected from the following:

(a) phenyl optionally substituted with one, two or three substituents independently selected from

(a-1) halo,  $C_{1-4}$  alkyl, halo-substituted  $C_{1-4}$  alkyl, OH,  $C_{1-4}$  alkoxy, halo-

- substituted  $C_{1-4}$  alkoxy,  $C_{1-4}$  alkylthio,  $NO_2$ ,  $NH_2$ , di- $(C_{1-4}$  alkyl)amino,  $C_{1-4}$  alkylamino, CN, HO-( $C_{1-4}$ ) alkyl,  $C_{1-4}$  alkoxy- $C_{1-4}$  alkyl,  $C_{1-4}$  alkylsulfonyl, aminosulfonyl,  $-NH_2S(O)_2NR^2R^3$ , acetyl,  $-COOH$ ,  $-C(O)O-C_{1-4}$  alkyl,  $C_{1-4}$  alkylsulfonylamino and  $C_{3-7}$  cycloalkyl,
- 5 (a-2) aryl or  $-O-(CH_2)_n$ -aryl, and the aryl or aryl moiety being optionally substituted with one, two or three substituents independently selected from halo,  $C_{1-4}$  alkyl, halo-substituted  $C_{1-4}$  alkyl, OH,  $C_{1-4}$  alkoxy, halo-substituted  $C_{1-4}$  alkoxy,  $C_{1-4}$  alkylthio,  $NO_2$ ,  $NH_2$ , di- $(C_{1-4}$  alkyl)amino,  $C_{1-4}$  alkylamino and CN,
- 10 (a-3) 5-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo,  $C_{1-4}$  alkyl, halo-substituted  $C_{1-4}$  alkyl, OH,  $C_{1-4}$  alkoxy, halo-substituted  $C_{1-4}$  alkoxy,  $C_{1-4}$  alkylthio,  $NO_2$ ,  $NH_2$ , di- $(C_{1-4}$  alkyl)amino,  $C_{1-4}$  alkylamino and CN,
- 15 (a-4) 6-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo,  $C_{1-4}$  alkyl, halo-substituted  $C_{1-4}$  alkyl, OH,  $C_{1-4}$  alkoxy, halo-substituted  $C_{1-4}$  alkoxy,  $C_{1-4}$  alkylthio,  $NO_2$ ,  $NH_2$ , di- $(C_{1-4}$  alkyl)amino,  $C_{1-4}$  alkylamino and CN,
- 20 (b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),
- 25 (c) a 5-membered monocyclic aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);
- 30 (d)  $C_{3-7}$  cycloalkyl optionally substituted with one or two substituents

independently selected from OH, C<sub>1-4</sub> alkyl, halo and halo-substituted C<sub>1-4</sub> alkyl; and

- (e) a benzo-fused heterocycle optionally substituted with one, two or three substituents independently selected from the group (a-1);

5 R<sup>1</sup> is hydrogen, C<sub>1-4</sub> alkyl or halo;

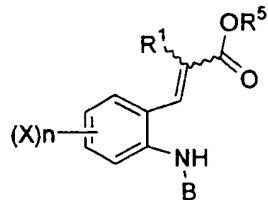
R<sup>2</sup> and R<sup>3</sup> are independently H, OH, C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkyl substituted with halo, OH, C<sub>1-4</sub> alkoxy, NH<sub>2</sub> or CN;

R<sup>5</sup> is C<sub>1-6</sub> alkyl;

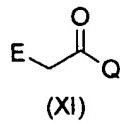
X is independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>NR<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl; and

n is 0, 1, 2, 3 or 4,

15 which process comprises reacting a compound of the formula (IX):



wherein R<sup>1</sup>, R<sup>5</sup>, X, and n are as defined above, and B is a suitable protecting group, with a compound of the formula (XI):



20 wherein E is halo and Q is as defined as before,

in the presence of a suitable base at a temperature of -40 °C to 200 °C to obtain a compound of the formula (XII).

69. A process according to Claim 68, wherein the reaction is carried out at a temperature of 0 °C to 100 °C

70. A process according to Claim 68, wherein the suitable base is potassium carbonate, cesium carbonate, sodium carbonate, sodium *tert*-butoxide, potassium *tert*-butoxide, sodium hydride, potassium hydride or potassium fluoride.

71. A process according to Claim 68, wherein the reaction is firstly carried out in the presence of a base for 2 minutes to a day; and then, another base is added to the reaction mixture.

72. A process according to Claim 71, wherein the reaction is firstly carried out for 30 minutes to 8 hours.

73. A process according to claims 67 and 68, wherein the suitable protecting group is methoxycarbonyl, ethoxycarbonyl, *tert*-butoxycarbonyl, benzyloxycarbonyl, phenylsulfonyl, p-toluenesulfonyl, methanesulfonyl or trifluoromethanesulfonyl.

74. A process according to claim 73, wherein the suitable protecting group is phenylsulfonyl, p-toluenesulfonyl, methanesulfonyl or trifluoromethanesulfonyl.

75. A process according to claim 71, wherein the first base is selected from sodium *tert*-butoxide, potassium *tert*-butoxide, sodium carbonate, potassium carbonate, cesium carbonate, sodium hydride, potassium hydride, sodium carbonate, potassium carbonate, cesium carbonate, potassium fluoride, 1,8-diazabicyclo[5.4.0]undec-7-ene, 1,5-diazabicyclo[4.3.0]non-5-ene, 1,4-diazabicyclo[2.2.2]octane, pyridine, pyrrolidine, triethylamine, diisopropylamine, diisopropylethylamine and diethylisopropylamine and

the second base is selected from sodium *tert*-butoxide, potassium *tert*-butoxide, sodium carbonate, potassium carbonate, cesium carbonate, sodium hydride, potassium hydride, sodium carbonate, potassium carbonate, cesium carbonate, potassium fluoride, 1,8-diazabicyclo[5.4.0]undec-7-ene, 1,5-diazabicyclo[4.3.0]non-5-ene, 1,4-diazabicyclo[2.2.2]octane, pyridine, pyrrolidine, triethylamine, diisopropylamine, diisopropylethylamine and diethylisopropylamine.

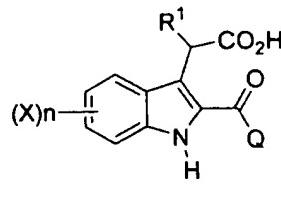
76. A process according to claim 75, wherein the first base is selected from potassium carbonate, cesium carbonate, sodium hydride and potassium fluoride; and the second base is selected from 1,8-diazabicyclo[5.4.0]undec-7-ene, cesium carbonate, pyrrolidine, diisopropylamine, triethylamine, diethylisopropylamine and diisopropylethylamine.

77. A process according to claim 75, wherein the first base is potassium carbonate, cesium carbonate or potassium fluoride; and the second base is 1,8-diazabicyclo[5.4.0]undec-7-ene, potassium tert-butoxide or cesium carbonate.

78. A process according to claim 77, wherein the combination of the first base and the second base (first base/second base) is selected from potassium carbonate/1,8-diazabicyclo[5.4.0]undec-7-ene, potassium carbonate/cesium carbonate, cesium carbonate/potassium tert-butoxide, cesium carbonate/1,8-diazabicyclo[5.4.0]undec-7-ene and potassium fluoride/1,8-diazabicyclo[5.4.0]undec-7-ene and potassium fluoride/cesium carbonate.

79. A process according to claim 78, wherein the combination of the first base and the second base (first base/second base) is selected from potassium carbonate/1,8-diazabicyclo[5.4.0]undec-7-ene, potassium carbonate/cesium carbonate and cesium carbonate/potassium tert-butoxide.

80. A process for preparing a compound of the formula (VIII):



(VIII)

15

wherein

**Q** is selected from the following:

- (a) phenyl optionally substituted with one, two or three substituents independently selected from
  - (a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>R<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl,
  - (a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub>

alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

5 (a-3) 5-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

10

(a-4) 6-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

15

(b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),

20

(c) a 5-membered monocyclic aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);

25

(d) C<sub>3-7</sub> cycloalkyl optionally substituted with one or two substituents independently selected from OH, C<sub>1-4</sub> alkyl, halo and halo-substituted C<sub>1-4</sub> alkyl; and

(e) a benzo-fuzed heterocycle optionally substituted with one, two or three substituents independently selected from the group (a-1);

R<sup>1</sup> is hydrogen, C<sub>1-4</sub> alkyl or halo;

30

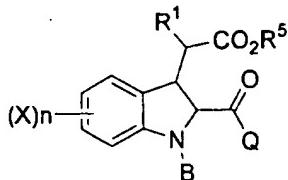
R<sup>2</sup> and R<sup>3</sup> are independently H, OH, C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkyl substituted with halo, OH, C<sub>1-4</sub> alkoxy, NH<sub>2</sub> or CN;

X is independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub>

alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>NR<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl; and

5    n is 0, 1, 2, 3 or 4,

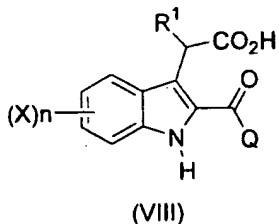
which process comprises treating a compound of the formula (X):



(X)

wherein R<sup>1</sup>, R<sup>5</sup>, X, Q and n are as defined here before, with a suitable base under hydrolyzing conditions to obtain the compound of formula (VIII).

10    81. A process for preparing a compound of the formula (VIII):



wherein

Q is selected from the following:

- (a) phenyl optionally substituted with one, two or three substituents independently selected from
  - (a-1) halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>NR<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl,
  - (a-2) aryl or -O-(CH<sub>2</sub>)<sub>n</sub>-aryl, and the aryl or aryl moiety being optionally substituted with one, two or three substituents independently

selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

(a-3) 5-membered monocyclic aromatic group optionally substituted with  
5 one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

10 (a-4) 6-membered monocyclic aromatic group optionally substituted with one, two or three substituents independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkyl)amino, C<sub>1-4</sub> alkylamino and CN,

15 (b) a 6-membered monocyclic aromatic group containing one, two, three or four nitrogen atom(s), and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4),

20 (c) a 5-membered monocyclic aromatic group containing one heteroatom selected from O, S and N and optionally containing one, two or three nitrogen atom(s) in addition to said heteroatom, and said monocyclic aromatic group being optionally substituted with one, two or three substituents independently selected from the above group (a-1), (a-2), (a-3) and (a-4);

25 (d) C<sub>3-7</sub> cycloalkyl optionally substituted with one or two substituents independently selected from OH, C<sub>1-4</sub> alkyl, halo and halo-substituted C<sub>1-4</sub> alkyl; and

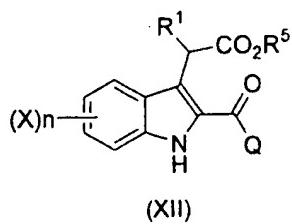
(e) a benzo-fuzed heterocycle optionally substituted with one, two or three substituents independently selected from the group (a-1);

R<sup>1</sup> is hydrogen, C<sub>1-4</sub> alkyl or halo;

30 R<sup>2</sup> and R<sup>3</sup> are independently H, OH, C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkyl substituted with halo, OH, C<sub>1-4</sub> alkoxy, NH<sub>2</sub> or CN;

X is independently selected from halo, C<sub>1-4</sub> alkyl, halo-substituted C<sub>1-4</sub> alkyl, OH, C<sub>1-4</sub> alkoxy, halo-substituted C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, NO<sub>2</sub>, NH<sub>2</sub>, di-(C<sub>1-4</sub> alkylamino), C<sub>1-4</sub> alkylamino, CN, HO-(C<sub>1-4</sub>) alkyl, C<sub>1-4</sub> alkoxy-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonyl, aminosulfonyl, -NH<sub>2</sub>S(O)<sub>2</sub>NR<sup>2</sup>NR<sup>3</sup>, acetyl, -COOH, -C(O)O-C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylsulfonylamino and C<sub>3-7</sub> cycloalkyl; and  
5 n is 0, 1, 2, 3 or 4,

which process comprises hydrolyzing a compound of the formula (XII):



wherein R<sup>5</sup> is C<sub>1-6</sub> alkyl, R<sup>1</sup>, X, Q and n are as defined herein before.

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 98/02065

A. CLASSIFICATION OF SUBJECT MATTER					
IPC 6	C07D209/18	A61K31/40	C07D401/06	C07D403/06	C07D417/06
	C07D405/06	C07D409/10	C07D405/10	C07D401/10	C07D417/10
	C07D413/06	C07D409/06			

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 510 368 A (MERCK FROSST CANADA INC.) 23 April 1996 cited in the application see claims -----	1,18
A	WO 96 37469 A (MERCK FROSST CANADA INC.) 28 November 1996 cited in the application see claims -----	1,18

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

### \* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority, claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

19 February 1999

26/02/1999

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
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Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.  
Fax: (+31-70) 340-3016

Authorized officer

Van Bijlen, H

**INTERNATIONAL SEARCH REPORT**

International application No

PCT/IB 98/02065

**B x I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: 35 because they relate to subject matter not required to be searched by this Authority, namely:  
**Remark:** Although claim 35 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

- The additional search fees were accompanied by the applicant's protest  
 No protest accompanied the payment of additional search fees.

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No	
PCT/IB 98/02065	

Patent document cited in search report	Publication date	Patent family member(s)			Publication date
US 5510368	A 23-04-1996	AU 5683196 A			11-12-1996
		CA 2219115 A			28-11-1996
		WO 9637468 A			28-11-1996
WO 9637469	A 28-11-1996	US 5604253 A			18-02-1997
		AU 5683296 A			11-12-1996
		CA 2219111 A			28-11-1996

PCT

世界知的所有権機関  
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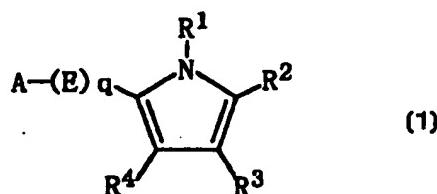
## 特許協力条約に基づいて公開された国際出願



(51) 国際特許分類6 A61K 31/40 // C07D 207/34	A1	(11) 国際公開番号 <b>WO99/61016</b>
		(43) 国際公開日 1999年12月2日(02.12.99)
(21) 国際出願番号 PCT/JP99/02763		
(22) 国際出願日 1999年5月26日(26.05.99)		
(30) 優先権データ 特願平10/145518 1998年5月27日(27.05.98) JP		
(71) 出願人 (米国を除くすべての指定国について) 日本新薬株式会社(NIPPON SHINYAKU CO., LTD.)[JP/JP] 〒601-8550 京都府京都市南区吉祥院西ノ庄門口町14番地 Kyoto, (JP)		(81) 指定国 AU, BG, BR, CA, CN, CZ, HU, ID, IL, JP, KR, LK, MN, MX, NO, NZ, PL, RU, SG, SK, UA, US, VN, 欧州特許 (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), ヨーラシア特許 (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM)
(72) 発明者; および (75) 発明者/出願人 (米国についてのみ) 田中充士(TANAKA, Mitsushi)[JP/JP] 〒520-3223 滋賀県甲賀郡甲西町夏見1513 Shiga, (JP) 津田正己(TSUDA, Masami)[JP/JP] 〒610-0112 京都府城陽市長池北清水64-88 Kyoto, (JP) 中村文胤(NAKAMURA, Ayatsugu)[JP/JP] 〒630-8224 奈良県奈良市三条町606-76 奈良ハイタウン5-203 Nara, (JP)		添付公開書類 国際調査報告書

(54) Title: CYCLOOXYGENASE-2 INHIBITORS

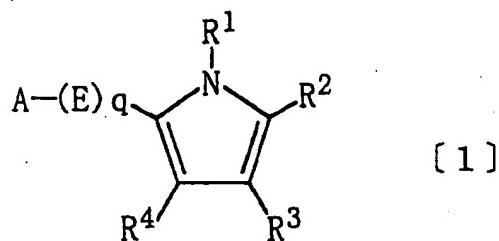
(54) 発明の名称 シクロオキシゲナーゼ2阻害剤



## (57) Abstract

Medicinal compositions containing as the active ingredient pyrrole derivatives represented by general formula (1) or pharmaceutically acceptable salts thereof. In said formula, R<sup>1</sup> represents hydrogen or alkoxy carbonylamino; R<sup>2</sup> represents alkyl, optionally substituted aryl, optionally substituted heteroaryl, unsubstituted amino, monoalkylated amino, dialkylated amino or optionally substituted cyclic amino; R<sup>3</sup> represents cyano or carbamoyl; R<sup>4</sup> represents hydrogen or alkyl; E represents alkylene; q is 0 or 1; and A represents methyl, optionally substituted aryl or optionally substituted heteroaryl. These compositions are useful as cyclooxygenase-2 inhibitors.

本発明は、次の式 [1]



(式中、R<sup>1</sup>は水素又はアルコキシカルボニルアミノを表す。R<sup>2</sup>は、アルキル、置換されていてもよいアリール、置換されていてもよい芳香族複素環基、無置換アミノ、モノアルキル置換アミノ、ジアルキル置換アミノ、又は置換されていてもよい環状アミノを表す。R<sup>3</sup>はシアノ又はカルバモイルを表す。R<sup>4</sup>は水素又はアルキルを表す。Eはアルキレンを表す。qは0又は1を表す。Aは、メチル、置換されていてもよいアリール、又は置換されていてもよい芳香族複素環基を表す。)で表されるピロール誘導体又はその薬学的に許容される塩を有効成分とする医薬組成物で構成される。本発明医薬組成物は、シクロオキシゲナーゼ-2阻害剤として有用である。

PCTに基づいて公開される国際出願のパンフレット第一頁に掲載されたPCT加盟国を同定するために使用されるコード(参考情報)

AE	アラブ首長国連邦	DM	ドミニカ	KZ	カザフスタン	RU	ロシア
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## 明細書

## シクロオキシゲナーゼー 2 阻害剤

## 技術分野

本発明は、ピロール誘導体又はその薬学的に許容される塩を有効成分とするシクロオキシゲナーゼー 2 阻害剤に関する。シクロオキシゲナーゼー 2 阻害剤は、シクロオキシゲナーゼー 2 が関与する生理学的障害の予防又は治療に有用である。

## 背景技術

シクロオキシゲナーゼは、プロスタグランジン類(以下、PG という)産生系における律速酵素である。近年、シクロオキシゲナーゼには、シクロオキシゲナーゼー 1 (COX-1)、シクロオキシゲナーゼー 2 (COX-2) と呼ばれる 2 つのアイソザイムが存在することが知られるようになった。

シクロオキシゲナーゼー 1 は、胃粘膜、精囊腺、血小板、腎臓等の細胞において常に発現しており、生体の恒常性維持に関与していると考えられている。

これに対して、シクロオキシゲナーゼー 2 は、マクロファージや滑膜細胞等の炎症に関する細胞をサイトカイン等で刺激することにより誘導されることから、炎症反応に深く関与すると考えられており、シクロオキシゲナーゼー 2 を阻害する化合物は、抗炎症鎮痛剤として期待されている。また、慢性疼痛や、無害な触覚刺激までもが痛みになる異痛にシクロオキシゲナーゼー 2 により產生された PG が関与することが報告されており、シクロオキシゲナーゼー 2 阻害剤はこれらの疼痛に対しても有効であると考えられている。

さらに、近年、骨芽細胞に誘導されたシクロオキシゲナーゼー 2 により产生された PG が、破骨細胞を活性化して骨吸收を引き起こすことが明らかにされ、骨吸收又は骨破壊を伴う疾患(例えば骨粗鬆症、慢性関節リウマチ、変形性関節症)へのシクロオキシゲナーゼー 2 阻害剤の適用が期待されている。さらにまた、シクロオキシゲナーゼー 2 阻害剤は、ホルモンにより誘発される子宮収縮を阻害するであろうし、アルツハイマー病における神経脱落や脳血管障害における神經壞死を抑制するであろうし、抗癌効果を示すであろうと考えられている。

これまで、本発明に係るピロール誘導体(以下、本発明化合物といふ)が頻尿・尿失禁治療作用を有することが知られていた(国際公開WO96/40634号公報)が、

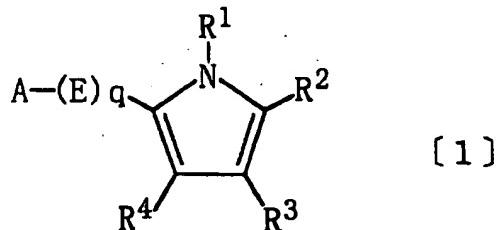
シクロオキシゲナーゼ-2阻害作用を有することは知られていない。

### 発明の開示

本発明の目的は、新規なシクロオキシゲナーゼ-2阻害剤を提供することにある。

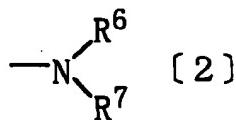
5 本発明者らは、種々の化合物について鋭意検討したところ、思いがけず、下記一般式〔1〕で表されるピロール誘導体がシクロオキシゲナーゼ-2阻害作用を有することを見出して本発明を完成した。

本発明は、次の一般式〔1〕で表されるピロール誘導体又はその薬学的に許容される塩を有効成分とするシクロオキシゲナーゼ-2阻害剤である。



10 式中、R<sup>1</sup>は水素又はアルコキシカルボニルアミノを表す。

R<sup>2</sup>は、(i)アルキル、(ii)置換されていてもよいアリール、(iii)置換されていてもよい芳香族複素環基、(iv)次の式〔2〕で表される基

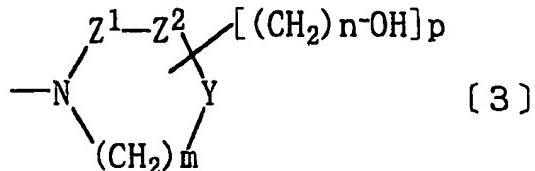


15

[式中、R<sup>6</sup>、R<sup>7</sup>は同一又は異なって、(1)水素又は(2)アルキル（かかるアルキルは(1)アルコキシで置換されていてもよいアリール、(2)芳香族複素環基、又は(3)ヒドロキシのいずれかで置換されていてもよい。）を表す。]

又は(v)次の式〔3〕で表される基

20



[式中、Z<sup>1</sup>、Z<sup>2</sup>は同一又は異なって-CH<sub>2</sub>-又は>C=Oを表す。但し、Z<sup>1</sup>、

$Z^2$ 共に  $>C=O$  の場合を除く。Yは  $-CH_2-$ 、 $-O-$ 、 $-S-$  又は  $>NR^9$  を表す。R<sup>9</sup>は水素、アルキル、アシル、アリール又は芳香族複素環基を表す。mは1～3の整数を表し、nは0～2の整数を表し、pは0又は1を表す。]を表す。

5 R<sup>2</sup>が置換されているアリール又は置換されている芳香族複素環基を表す場合、かかる置換基としては、(1)ハロゲン、(2)ハロゲンで置換されていてもよいアルキル、(3)シアノ、(4)ニトロ、(5)アルコキシカルボニル、(6)ヒドロキシ、(7)アルコキシ(かかるアルコキシは(1)ハロゲン、(2)アルコキシで置換されていてもよいアリール又は(3)アルコキシのいずれかで置換されていてもよい。)、

10 (8)-NHSO<sub>2</sub>R<sup>82</sup>及び(9)-NR<sup>83</sup>R<sup>84</sup>からなる群から、同一又は異なるものが1個～3個選ばれる。又は2個の隣接した置換基が一緒になって、  
 $-O-(CH_2)_t-O-$ (tは1又は2を表す。)を表してもよい。

R<sup>82</sup>は、(1)アルキル又は(2)アルキルで置換されていてもよいアリールを表す。

15 R<sup>83</sup>、R<sup>84</sup>は同一又は異なって、(1)水素、(2)アルキル又は(3)アシルを表す。又はR<sup>83</sup>、R<sup>84</sup>は隣接するNと一緒にになって5員環～7員環の環状アミノを表す。

R<sup>3</sup>はシアノ又はカルバモイルを表す。

R<sup>4</sup>は水素又はアルキルを表す。

Eはアルキレンを表し、qは0又は1を表す。

Aは、(1)メチル、(2)置換されていてもよいアリール又は(3)置換されていてもよい芳香族複素環基のいずれかを表す。

20 Aが置換されているアリール又は置換されている芳香族複素環基を表す場合、かかる置換基としては、(1)ハロゲン、(2)ハロゲンで置換されていてもよいアルキル、(3)シアノ、(4)ニトロ、(5)アルコキシカルボニル、(6)ヒドロキシ、(7)アルコキシ(かかるアルコキシは(1)ハロゲン、(2)アルコキシで置換されていてもよいアリール又は(3)アルコキシのいずれかで置換されていてもよい。)、

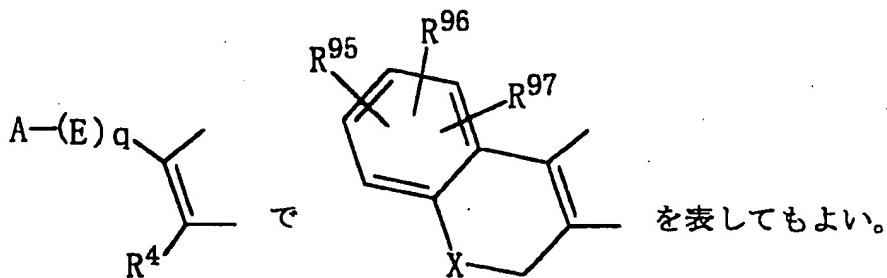
25 (8)-NHSO<sub>2</sub>R<sup>92</sup>及び(9)-NR<sup>93</sup>R<sup>94</sup>からなる群から、同一又は異なるものが1個～3個選ばれる。又は2個の隣接した置換基が一緒になって、

$-O-(CH_2)_u-O-$ (uは1又は2を表す。)を表してもよい。

R<sup>92</sup>は、(1)アルキル又は(2)アルキルで置換されていてもよいアリールを表す。

R<sup>93</sup>、R<sup>94</sup>は同一又は異なって、(1)水素、(2)アルキル又は(3)アシルを表す。又はR<sup>93</sup>、R<sup>94</sup>は隣接するNと一緒にになって5員環～7員環の環状アミノを表す。

また、A-(E)-q、R<sup>4</sup>及びピロール環の二重結合は一緒になって、



10 Xは-O-、-S-又は>NR<sup>90</sup>を表す。R<sup>90</sup>はアルキルを表す。

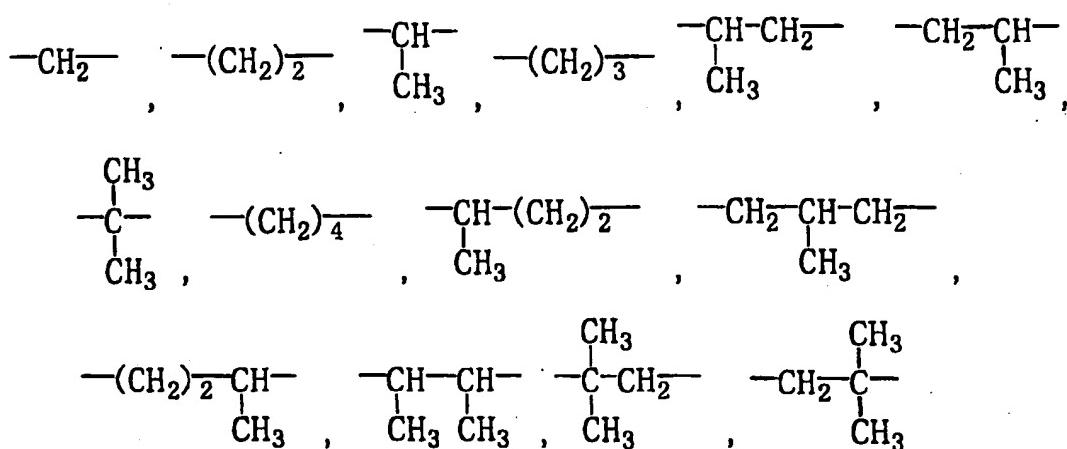
R<sup>95</sup>、R<sup>96</sup>、R<sup>97</sup>は同一又は異なって、(1)水素、(2)ハロゲン、(3)ハロゲンで置換されていてもよいアルキル、(4)シアノ、(5)ニトロ、(6)アルコキシカルボニル、(7)ヒドロキシ、(8)アルコキシ(かかるアルコキシはハロゲン又はアルコキシで置換されていてもよい。)、(9)-NHSO<sub>2</sub>R<sup>92</sup>(R<sup>92</sup>は前記と同じ。)及び(10)-NR<sup>93</sup>R<sup>94</sup>(R<sup>93</sup>、R<sup>94</sup>は前記と同じ。)からなる群から選ばれる。また、R<sup>95</sup>、R<sup>96</sup>、R<sup>97</sup>のいずれか2個の隣接した置換基が一緒になって、-O-(CH<sub>2</sub>)<sub>u</sub>-O-(uは前記と同じ。)を表してもよい。

20 本発明において、「アルキル」としては、直鎖状又は分枝鎖状の炭素数1～4のもの、例えば、メチル、エチル、n-プロピル、イソプロピル、n-ブチル、イソブチル、sec-ブチル、tert-ブチルが挙げられる。

「アリール」としては、炭素数6～12のもの、例えば、フェニル、1-ナフチル、2-ナフチル、3-ビフェニル、4-ビフェニルが挙げられる。

25 「芳香族複素環基」としては、窒素、酸素又は硫黄を1～4個含む芳香族の5～6員環又はそれらのベンゼン縮合環(但し、2-ピロリル及び3-ピロリルを除く。)、例えば、2-ピリジル、3-ピリジル、4-ピリジル、2-ピリミジニル、4-ピリミジニル、1-インドリル、2-インドリル、3-インドリル、1-テトラゾリル、2-フリル、3-フリル、2-ベンゾフラニル、3-ベンゾフラニル、2-チエニル、3-チエニルが挙げられる。

「アルキレン」としては、直鎖状又は分枝鎖状の炭素数1～4のもの、例えば、次のものが挙げられる。



10 「アルコキシ」、「アルコキシカルボニル」又は「アルコキシカルボニルアミノ」のアルキル部分としては、上記で例示したアルキルが挙げられる。

「ハロゲン」としては、例えば、フッ素、塩素、臭素、ヨウ素が挙げられる。

「アシリル」としては、炭素数1～7のもの、例えば、ホルミル、アセチル、ブロピオニル、ブチリル、イソブチリル、バレリル、インバレリル、ピバロイル、ヘキサノイル、イソヘキサノイル、ベンゾイルが挙げられる。

NR<sup>83</sup>R<sup>84</sup>、NR<sup>93</sup>R<sup>94</sup>で示される5員環～7員環の環状アミノとしては、例えば、1-ピロリジニル、1-ピペリジニル、1-ヘキサメチレンイミノが挙げられる。

本発明化合物〔1〕の中で好ましい化合物としては、例えば、R<sup>1</sup>が水素、R<sup>2</sup>がNH<sub>2</sub>、モノアルキルアミノ又はジアルキルアミノ、R<sup>3</sup>がシアノ、R<sup>4</sup>が水素又はメチル、Aが置換されていてもよいアリール又は置換されていてもよい芳香族複素環基、qが0である化合物が挙げられる。

本発明化合物〔1〕の中で特に好ましい化合物としては、例えば、次の(1)～(9)の化合物が挙げられる。

- 25 (1) 2-アミノ-3-シアノ-5-(2-フルオロフェニル)-4-メチルピロール(以下、化合物1という)、  
 (2) 2-アミノ-3-シアノ-4-メチル-5-フェニルピロール(以下、化合物2という)、  
 (3) 2-アミノ-5-(2,5-ジクロロフェニル)-3-シアノ-4-メチル

ピロール(以下、化合物3という)、

(4) 2-(n-ブチルアミノ)-3-シアノ-5-(4-フルオロフェニル)-4-メチルピロール(以下、化合物4という)、

(5) 2-アミノ-3-シアノ-5-フェニルピロール(以下、化合物5という)、

5 (6) 2-アミノ-3-シアノ-5-(4-エトキシフェニル)-4-メチルピロール(以下、化合物6という)、

(7) 2-アミノ-3-シアノ-5-(4-フルオロフェニル)ピロール(以下、化合物7という)、

10 (8) 2-ジメチルアミノ-3-シアノ-5-フェニル-4-メチルピロール(以下、化合物8という)、

(9) 2-アミノ-3-シアノ-5-(2, 5-ジフルオロフェニル)-4-メチルピロール。(以下、化合物9という)。

15 上記式〔1〕で表される本発明化合物は、国際公開WO96/40634号公報に記載された方法により製造することができる。

本発明化合物の中で塩基性を示す化合物は、遊離の塩基のまま医薬として用いることができるが、公知の方法により薬学的に許容される塩の形にして医薬として用いることができる。塩としては、塩酸、臭化水素酸、硫酸、磷酸などの鉱酸の塩、酢酸、クエン酸、酒石酸、マレイン酸、コハク酸、フマル酸、p-トルエンスルホン酸、ベンゼンスルホン酸、メタンスルホン酸などの有機酸の塩が挙げられる。

20 本発明化合物は、後記する試験例に示すように優れたシクロオキシゲナーゼ-2阻害作用を有しており、また毒性は低いので、炎症、疼痛、異痛、骨粗鬆症、慢性関節リウマチ、変形性関節症、ホルモン誘発子宮収縮、アルツハイマー病、脳血管障害、癌の予防又は治療に有用である。

25 本発明に係る化合物を医薬として投与する場合、本発明に係る化合物は、そのまま又は医薬的に許容される無毒性かつ不活性の担体中に、例えば0.1~99.5%、好ましくは0.5~90%を含有する医薬組成物として、人を含む哺乳動物に投与することができる。

担体としては、固形、半固形又は液状の希釈剤、充填剤及びその他の処方用の助剤一種以上が用いられる。医薬組成物は、投与単位形態で投与することが望ましい。本発明医薬組成物は、静脈内投与、経口投与、組織内投与、局所投与（経皮投与など）又は経直腸的に投与することができる。これらの投与方法に適した5 剂型で投与されるのはもちろんである。経口投与が特に好ましい。

経口投与は固形又は液状の用量単位、例えば、末剤、散剤、錠剤、糖衣剤、カプセル剤、顆粒剤、懸濁剤、液剤、シロップ剤、ドロップ剤、舌下錠その他の剤型によって行うことができる。

10 末剤は活性物質を適當な細かさにすることにより製造される。散剤は活性物質を適當な細かさと成し、ついで同様に細かくした医薬用担体、例えば澱粉、マンニトールのような可食性炭水化物その他と混合することにより製造される。必要に応じ風味剤、保存剤、分散剤、着色剤、香料その他のものを混じてもよい。

15 カプセル剤は、まず上述のようにして粉末状となつた末剤や散剤又は錠剤の項で述べるように顆粒化したものを、例えばゼラチンカプセルのようなカプセル外皮の中へ充填することにより製造される。滑沢剤や流動化剤、例えばコロイド状のシリカ、タルク、ステアリン酸マグネシウム、ステアリン酸カルシウム、固形のポリエチレングリコールのようなものを粉末状態のものに混合し、然るのちに充填操作を行うこともできる。崩壊剤や可溶化剤、例えばカルボキシメチルセルロース、カルボキシメチルセルロースカルシウム、低置換度ヒドロキシプロピルセルロース、クロスカルメロースナトリウム、カルボキシメチルスターーナトリウム、炭酸カルシウム、炭酸ナトリウムを添加すれば、カプセル剤が摂取されたときの医薬の有効性を改善することができる。

20 また、本品の微粉末を植物油、ポリエチレングリコール、グリセリン、界面活性剤中に懸濁分散し、これをゼラチンシートで包んで軟カプセル剤とすることが可能である。錠剤は賦形剤を加えて粉末混合物を作り、顆粒化もしくはスラグ化し、ついで崩壊剤又は滑沢剤を加えたのち打錠することにより製造される。粉末混合物は、適当に粉末化された物質を上述の希釈剤やベースと混合し、必要に応じ結合剤（例えば、カルボキシメチルセルロースナトリウム、メチルセルロース、ヒドロキシプロピルメチルセルロース、ゼラチン、ポリビニルピロリドン、ポリビ

ニルアルコールなど)、溶解遅延化剤(例えば、パラフィンなど)、再吸収剤(例えば、四級塩)や吸着剤(例えばペントナイト、カオリン、リン酸ジカルシウムなど)をも併用して製造される。粉末混合物は、まず結合剤、例えばシロップ、澱粉糊、アラビアゴム、セルロース溶液又は高分子物質溶液で湿らせ、攪拌混合し、これを乾燥、粉碎して顆粒とすることができます。このように粉末を顆粒化するかわりに、まず打錠機にかけたのち、得られる不完全な形態のスラグを破碎して顆粒にすることも可能である。

10 このようにして作られる顆粒は、滑沢剤としてステアリン酸、ステアリン酸塩、タルク、ミネラルオイルその他を添加することにより、互いに付着することを防ぐことができる。このように滑沢化された混合物をついで打錠する。こうして製造した素錠にフィルムコーティングや糖衣を施すことができる。

15 また薬物は、上述のように顆粒化やスラグ化の工程を経ることなく、流動性の不活性担体と混合したのちに直接打錠してもよい。シェラックの密閉被膜からなる透明又は半透明の保護被覆、糖や高分子材料の被覆、及び、ワックスよりなる磨上被覆の如きも用いられる。

20 他の経口投与剤型、例えば溶液、シロップ、エリキシルなどもまたその一定量が薬物の一定量を含有するように用量単位形態にすることができる。シロップは、化合物を適当な香味水溶液に溶解して製造され、またエリキシルは非毒性のアルコール性担体を用いることにより製造される。懸濁剤は、化合物を非毒性担体中に分散させることにより処方される。可溶化剤や乳化剤(例えば、エトキシ化されたイソステアリルアルコール類、ポリオキシエチレンソルビールエステル類)、保存剤、風味賦与剤(例えば、ペパミント油、サッカリン)その他もまた必要に応じ添加することができる。

25 必要とあらば、経口投与のための用量単位処方はマイクロカプセル化してもよい。該処方はまた被覆をしたり、高分子・ワックス等中にうめこんだりすることにより作用時間の延長や持続放出をもたらすこともできる。

組織内投与は、皮下・筋肉又は静脈内注射用としたところの液状用量単位形態、例えば溶液や懸濁剤の形態を用いることによって行うことができる。これらのものは、化合物の一定量を、注射の目的に適合する非毒性の液状担体、例えば水性

や油性の媒体に懸濁し又は溶解し、ついで該懸濁液又は溶液を滅菌することにより製造される。注射液を等張にするために非毒性の塩や塩溶液を添加してもよい。更に、安定剤、保存剤、乳化剤のようなものを併用することもできる。

直腸投与は、化合物を低融点の水に可溶又は不溶の固体、例えばポリエチレン

5 グリコール、カカオ脂、半合成の油脂（例えば、ウイテプゾール、登録商標）、高級エステル類（例えばパルミチン酸ミリスチルエステル）及びそれらの混合物に溶解又は懸濁させて製造した坐剤などを用いることによって行うことができる。

シクロオキシゲナーゼー2阻害剤としての用量は、病気の性質と程度、年齢、体重などの患者の状態、投与経路などを考慮した上で設定することが望ましいが、  
10 通常は、成人に対して本発明に係る化合物の有効成分量として、1日あたり、0.1～1000mg／ヒトの範囲、好ましくは1～500mg／ヒトの範囲が一般的である。

場合によっては、これ以下で足りるし、また逆にこれ以上の用量を必要とする  
こともある。また1日2～3回に分割して投与することもできる。

#### 発明を実施するための最良の形態

15 以下に試験例及び製剤例を掲げて本発明を更に詳しく説明するが、本発明はこれらのみに限定されるものではない。

#### 試験例 1

##### シクロオキシゲナーゼー2阻害作用

40 units/mlのヒツジ胎盤由来精製シクロオキシゲナーゼー2を用い、2μMヘマチン、2μM [1-<sup>14</sup>C]-アラキドン酸及び5mMトリプトファンを含む0.1Mトリス塩酸緩衝液を被験薬物と共に25°Cで6分間インキュベートした。0.2Mクエン酸緩衝液を加え反応を停止した後、反応液中の放射性物質を酢酸エチルで抽出し薄層板にて展開分離し、薄層板上の[1-<sup>14</sup>C]-アラキドン酸の放射活性をバイオイメージングアナライザーにて測定した。<sup>[1-14C]</sup>-アラキドン酸の消費量をPGの生合成量とし、その抑制率をシクロオキシゲナーゼー2抑制率とした。シクロオキシゲナーゼー2を50%阻害する被験薬物の濃度(IC<sub>50</sub>値)を、直線回帰分析法により算出した。

結果を表1に示す。

表 1 COX-2に対する作用

	使用 被験薬物	動物数	濃度(M)	抑制率(%)	IC <sub>50</sub> (M)
化合物 1	3	$5 \times 10^{-6}$	24.4	$7.3 \times 10^{-6}$	
	3	$1 \times 10^{-5}$	79.1		
	3	$2 \times 10^{-5}$	95.6		
化合物 2	3	$5 \times 10^{-6}$	16.4	$9.1 \times 10^{-6}$	
	3	$1 \times 10^{-5}$	61.7		
	3	$2 \times 10^{-5}$	86.3		
化合物 3	1	$1 \times 10^{-5}$	40.7		
化合物 4	1	$1 \times 10^{-5}$	33.0		
化合物 5	1	$1 \times 10^{-5}$	41.7		
化合物 6	1	$1 \times 10^{-5}$	29.5		
化合物 7	1	$1 \times 10^{-5}$	39.5		
化合物 8	1	$1 \times 10^{-5}$	58.9		
化合物 9	1	$1 \times 10^{-5}$	55.7		
イントメタシン	1	$3 \times 10^{-6}$	16.3	$1.0 \times 10^{-5}$	
	1	$1 \times 10^{-5}$	46.9		
	1	$3 \times 10^{-5}$	82.5		

本発明化合物が、イントメタシン相当以上の強さのシクロオキシゲナーゼー 2 阻害作用を有することが明白である。

### 試験例 2

#### 急性毒性試験

6-7 週齢の雄性 ddY系マウスを一群 4~5例として用いた。前日 (16-18時間前)

より絶食した後、ゾンデを用いて被験薬物を 1000mg/kg の投与量で強制的に経口投与し、以後 2週間における死亡例数の有無を観察した。被験薬物として、化合物 1、化合物 2、化合物 5、化合物 7、及び化合物 9 をそれぞれ投与した。

その結果、いずれの化合物投与群においても、死亡例は観察されなかった。

5 製剤例 1

錠剤（内服錠）

处方 1 錠200mg 中

化合物 1	20 mg
コーンスターク	88 mg
結晶セルロース	80 mg
カルボキシメチルセルロースカルシウム	10 mg
軽質無水ケイ酸	1 mg
ステアリン酸マグネシウム	1 mg

この割合で混合末を打錠成形し内服錠とする。

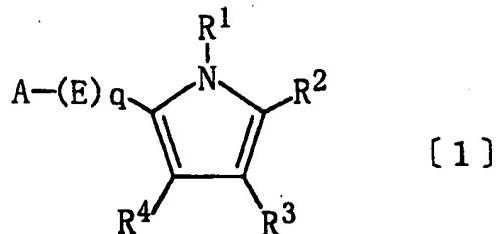
15 産業上の利用可能性

以上に示したように、本発明化合物は、優れたシクロオキシゲナーゼ-2 阻害作用を有し、毒性が低く安全な化合物であることから、本発明化合物を有効成分として含む医薬組成物は、ヒトを含む哺乳動物に対して、シクロオキシゲナーゼ-2 阻害剤として、炎症、疼痛、異痛、骨粗鬆症、慢性関節リウマチ、変形性関節症、ホルモン誘発子宮収縮、アルツハイマー病、脳血管障害、癌の予防又は治療に有用である。

## 請求の範囲

1. 次の式〔1〕で表されるピロール誘導体又はその薬学的に許容される塩を有効成分とするシクロオキシゲナーゼ-2阻害剤。

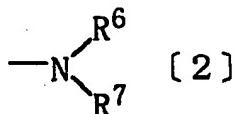
5



式中、R<sup>1</sup>は水素又はアルコキシカルボニルアミノを表す。

10 R<sup>2</sup>は、(i)アルキル、(ii)置換されていてもよいアリール、(iii)置換されていてもよい芳香族複素環基、(iv)次の式〔2〕で表される基

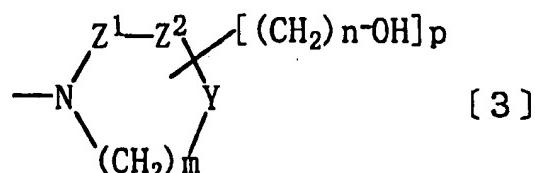
15



〔式中、R<sup>6</sup>、R<sup>7</sup>は同一又は異なって、(1)水素又は(2)アルキル(かかるアルキルは(1)アルコキシで置換されていてもよいアリール、(2)芳香族複素環基、又は(3)ヒドロキシのいずれかで置換されていてもよい。)を表す。〕

又は(v)次の式〔3〕で表される基

20



〔式中、Z<sup>1</sup>、Z<sup>2</sup>は同一又は異なって-CH<sub>2</sub>-又は>C=Oを表す。但し、Z<sup>1</sup>、Z<sup>2</sup>共に>C=Oの場合を除く。Yは-CH<sub>2</sub>-、-O-、-S-又は>NR<sup>9</sup>を表す。R<sup>9</sup>は水素、アルキル、アシル、アリール又は芳香族複素環基を表す。mは1~3の整数を表し、nは0~2の整数を表し、pは0又は1を表す。〕  
を表す。

R<sup>2</sup>が置換されているアリール又は置換されている芳香族複素環基を表す場合、

かかる置換基としては、(1)ハロゲン、(2)ハロゲンで置換されていてもよいアルキル、(3)シアノ、(4)ニトロ、(5)アルコキシカルボニル、(6)ヒドロキシ、(7)アルコキシ(かかるアルコキシは(1)ハロゲン、(2)アルコキシで置換されていてもよいアリール又は(3)アルコキシのいずれかで置換されていてもよい。)、

5 (8)-NHSO<sub>2</sub>R<sup>82</sup>及び(9)-NR<sup>83</sup>R<sup>84</sup>からなる群から、同一又は異なるものが1個～3個選ばれる。又は2個の隣接した置換基が一緒になって、

-O-(CH<sub>2</sub>)<sub>t</sub>-O-(tは1又は2を表す。)を表してもよい。

R<sup>82</sup>は、(1)アルキル又は(2)アルキルで置換されていてもよいアリールを表す。

10 R<sup>83</sup>、R<sup>84</sup>は同一又は異なって、(1)水素、(2)アルキル又は(3)アシルを表す。又はR<sup>83</sup>、R<sup>84</sup>は隣接するNと一緒にになって5員環～7員環の環状アミノを表す。

R<sup>3</sup>はシアノ又はカルバモイルを表す。

R<sup>4</sup>は水素又はアルキルを表す。

Eはアルキレンを表し、qは0又は1を表す。

Aは、(1)メチル、(2)置換されていてもよいアリール又は(3)置換されていてもよい芳香族複素環基のいずれかを表す。

20 Aが置換されているアリール又は置換されている芳香族複素環基を表す場合、かかる置換基としては、(1)ハロゲン、(2)ハロゲンで置換されていてもよいアルキル、(3)シアノ、(4)ニトロ、(5)アルコキシカルボニル、(6)ヒドロキシ、(7)アルコキシ(かかるアルコキシは(1)ハロゲン、(2)アルコキシで置換されていてもよいアリール又は(3)アルコキシのいずれかで置換されていてもよい。)、

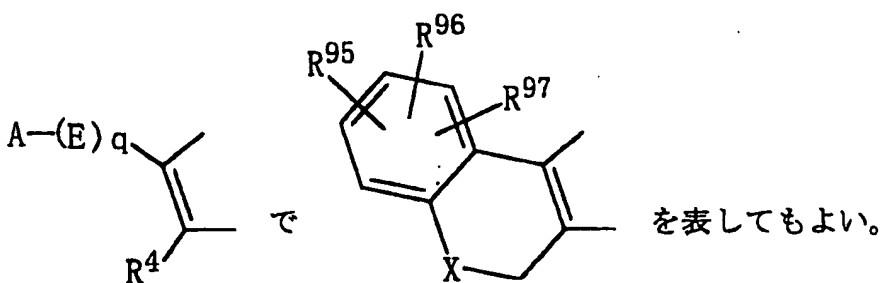
(8)-NHSO<sub>2</sub>R<sup>92</sup>及び(9)-NR<sup>93</sup>R<sup>94</sup>からなる群から、同一又は異なるものが1個～3個選ばれる。又は2個の隣接した置換基が一緒になって、

-O-(CH<sub>2</sub>)<sub>u</sub>-O-(uは1又は2を表す。)を表してもよい。

R<sup>92</sup>は、(1)アルキル又は(2)アルキルで置換されていてもよいアリールを表す。

25 R<sup>93</sup>、R<sup>94</sup>は同一又は異なって、(1)水素、(2)アルキル又は(3)アシルを表す。又はR<sup>93</sup>、R<sup>94</sup>は隣接するNと一緒にになって5員環～7員環の環状アミノを表す。

また、A-(E)<sub>q</sub>、R<sup>4</sup>及びピロール環の二重結合は一緒になって、



Xは-O-、-S-又は>NR<sup>90</sup>を表す。R<sup>90</sup>はアルキルを表す。

R<sup>95</sup>、R<sup>96</sup>、R<sup>97</sup>は同一又は異なって、(1)水素、(2)ハロゲン、(3)ハロゲンで置換されていてもよいアルキル、(4)シアノ、(5)ニトロ、(6)アルコキシカルボニル、  
10 (7)ヒドロキシ、(8)アルコキシ（かかるアルコキシはハロゲン又はアルコキシで置換されていてもよい。）、(9)-NH<sub>2</sub>SO<sub>2</sub>R<sup>92</sup>（R<sup>92</sup>は前記と同じ。）及び  
(10)-NR<sup>93</sup>R<sup>94</sup>（R<sup>93</sup>、R<sup>94</sup>は前記と同じ。）からなる群から選ばれる。また、  
R<sup>95</sup>、R<sup>96</sup>、R<sup>97</sup>のいずれか2個の隣接した置換基が一緒になって、  
-O-(CH<sub>2</sub>)<sub>u</sub>-O-（uは前記と同じ。）を表してもよい。

15 2. R<sup>1</sup>が水素、R<sup>2</sup>がNH<sub>2</sub>、R<sup>3</sup>がシアノ、R<sup>4</sup>が水素又はメチル、Aが置換されていてもよいアリール又は置換されていてもよい芳香族複素環基、qが0である請求項1記載のピロール誘導体又はその薬学的に許容される塩を有効成分とするシクロオキシゲナーゼ-2阻害剤。

20 3. ピロール誘導体が次のいずれかの化合物である請求項1記載のピロール誘導体又はその薬学的に許容される塩を有効成分とするシクロオキシゲナーゼ-2阻害剤。

- (1) 2-アミノ-3-シアノ-5-(2-フルオロフェニル)-4-メチルピロール、
- (2) 2-アミノ-3-シアノ-4-メチル-5-フェニルピロール、
- 25 (3) 2-アミノ-5-(2, 5-ジクロロフェニル)-3-シアノ-4-メチルピロール、
- (4) 2-(n-ブチルアミノ)-3-シアノ-5-(4-フルオロフェニル)-4-メチルピロール、
- (5) 2-アミノ-3-シアノ-5-フェニルピロール、

- (6) 2-アミノ-3-シアノ-5-(4-エトキシフェニル)-4-メチルピロール、  
(7) 2-アミノ-3-シアノ-5-(4-フルオロフェニル)ピロール、  
(8) 2-ジメチルアミノ-3-シアノ-5-フェニル-4-メチルピロール、  
5 (9) 2-アミノ-3-シアノ-5-(2, 5-ジフルオロフェニル)-4-メチルピロール。

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP99/02763

A. CLASSIFICATION OF SUBJECT MATTER  
Int.Cl<sup>6</sup> A61K31/40 // C07D207/34

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
Int.Cl<sup>6</sup> A61K31/40, C07D207/34

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
REGISTRY (STN), CA (STN), CAOLD (STN), CAPLUS (STN)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	WO, 98/02430, A1 (PFIZER PHARMACEUTICALS INC.), 22 January, 1998 (22. 01. 98), Particularly refer to Example 40 & EP, 912548, A1 & AU, 9730441, A1	1 2, 3
A	WO, 96/40634, A1 (Nippon Shinyaku Co., Ltd.), 19 December, 1996 (19. 12. 96) & EP, 842923, A1 & CA, 2223918, A & AU, 9659109, A1	1-3
A	JP, 09-323971, A (Sankyo Co., Ltd.), 16 December, 1997 (16. 12. 97) & EP, 799823, A1 & AU, 9716653, A & NO, 9701564, A & CA, 2201812, A & US, 5908858, A & KR, 97069985, A	1-3

 Further documents are listed in the continuation of Box C.  See patent family annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&amp;" document member of the same patent family

Date of the actual completion of the international search  
6 August, 1999 (06. 08. 99)Date of mailing of the international search report  
17 August, 1999 (17. 08. 99)Name and mailing address of the ISA/  
Japanese Patent Office

Authorized officer

Facsimile No.

Telephone No.

## A. 発明の属する分野の分類（国際特許分類（IPC））

Int. Cl° A61K31/40 // C07D207/34

## B. 調査を行った分野

## 調査を行った最小限資料（国際特許分類（IPC））

Int. Cl° A61K31/40, C07D207/34

## 最小限資料以外の資料で調査を行った分野に含まれるもの

## 国際調査で使用した電子データベース（データベースの名称、調査に使用した用語）

REGISTRY (STN), CA (STN), CAOLD (STN), CAPLUS (STN)

## C. 関連すると認められる文献

引用文献の カテゴリー*	引用文献名 及び一部の箇所が関連するときは、その関連する箇所の表示	関連する 請求の範囲の番号
X A	WO, 98/02430, A1 (PFIZER PHARMACEUTICALS INC.) 22. 1月. 1998(22. 01. 98) 特にExample40参照 &EP, 912548, A1 &AU, 9730441, A1	1 2, 3
A	WO, 96/40634, A1 (日本新薬株式会社) 19. 12月. 1996(19. 12. 96) &EP, 842923, A1 &CA, 2223918, A &AU, 9659109, A1	1-3
A	JP, 09-323971, A (三共株式会社) 16. 12月. 1997(16. 12. 97) &EP, 799823, A1 &AU, 9716653, A &NO, 9701564, A &CA, 2201812, A &US, 5908858, A &KR, 97069985, A	1-3

 C欄の続きにも文献が列挙されている。 パテントファミリーに関する別紙を参照。

## \* 引用文献のカテゴリー

「A」特に関連のある文献ではなく、一般的技術水準を示すもの

「E」国際出願日前の出願または特許であるが、国際出願日以後に公表されたもの

「L」優先権主張に疑義を提起する文献又は他の文献の発行日若しくは他の特別な理由を確立するために引用する文献（理由を付す）

「O」口頭による開示、使用、展示等に言及する文献

「P」国際出願日前で、かつ優先権の主張の基礎となる出願

## の日の後に公表された文献

「T」国際出願日又は優先日後に公表された文献であって出願と矛盾するものではなく、発明の原理又は理論の理解のために引用するもの

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「Y」特に関連のある文献であって、当該文献と他の1以上の文献との、当業者にとって自明である組合せによって進歩性がないと考えられるもの

「&amp;」同一パテントファミリー文献

## 国際調査を完了した日

06. 08. 99

## 国際調査報告の発送日

17.08.99

## 国際調査機関の名称及びあて先

日本国特許庁 (ISA/JP)

郵便番号 100-8915

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